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DIAPHRAGMATIC (HIATUS) HERNIA*

A Clinical Study

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DURING the last thirty years there has been published an extensive literature based on the study of large series of cases dealing with the signs, symptoms and differential diagnosis of hiatus hernia. Despite this, clinicians have been slow to appreciate the full importance of the disease, especially in the differential diagnosis of certain thoracic and abdominal conditions.

Any such point of view is not without medical literature to the contrary. As early as 1853, Bowditch[1] wrote a lengthy treatise on the subject of diaphragmatic hernia and reviewed the literature. The actual number of references in the literature was twenty-seven, beginning with the first reference to the disease made by Ambroise Paré in 1610. Bowditch carefully reviewed the symptomatology of the condition, which included most of the symptoms recognized today. Following the work of Bowditch, little appeared in the American literature until 1901, when Ingals[2] published an article entitled "The Diagnosis of Diaphragmatic Hernia." It is of considerable interest that the author mentions the following as the principal symptoms: dyspnea on exertion and sometimes on lying down, pain in the bowel, especially after a full meal and in cases in which the opening was small, and vomiting in many cases in which the opening was large.

PATHOLOGIC ANATOMY

Most observers conclude that all cases of diaphragmatic hernia are actually or essentially congenital in origin. Polley[3] suggests that age and obesity are contributing factors. He quotes other factors set forth by Akerlund as follows: stretching of the hiatus due to insufficiency of the surrounding muscle fibers, decrease in the amount of fat tissue in the esophageal ring, decrease in the elasticity of the elastic fibrous tissue about the hiatus, loosening of the connective tissue between the esophagus and the peritoneum and increase in intra-abdominal tension. In addition, Giffin[4] and Vinson[5] mention trauma or minor injuries; Ritvo[6] stresses increased abdominal tension and enumerates various causes; Turner,[7] and also Gaudrault and Chalmers,[8] suggest the production of hiatus hernia by increased abdominal pressure associated with neoplastic disease. Finally, Weintraub and Tuggle[9] mention the high incidence of diaphragmatic hernia in cases of duodenal diverticulum, concluding that if one congenital defect is found in the gastrointestinal tract, others are likely to be present.

SYMPTOMS

The symptoms of hiatus hernia may simulate any one of several conditions in either the anterior chest or upper abdomen. In describing this close relation Morton[10] aptly uses the term "mimic." Large series of cases have been reported by Giffin,[4] Hedblom,[11] Ritvo,[6] Dunhill,[12] Morrison,[13] Cowan,[14] Bock, Dulin and Brooke,[15] Harrington,[16] Dwyer,[17] Moersch,[18] Jenkinson and Roberts[19] Polley[3] and Jones.[20] Harrington[21] states that the symptoms may begin at birth or any time during life, and Ladd and Gross[22] call attention to the similarity of symptoms in children with those found in adults. In general, most authors agree that symptoms are more likely to occur in middle life, for reasons already stated.

Abdominal

From a review of certain articles in the literature (Cowan,[14] Hedblom[11] and Harrington,[23] it appears that the commonest abdominal symptoms,

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listed in order of frequency, are as follows: epigastric pain, a feeling of distress after or during a meal associated with bloating, belching and heartburn, nausea, vomiting and regurgitation, night pain or pain in the recumbent position, dysphagia and hiccough. Various methods for the relief of symptoms have been advocated, chief among which are getting up and walking about, induced vomiting, use of the stomach tube, defecation or use of enemas, alkalies and belladonna. Bock, Dulin and Brooke[15] mention the feeling as if a rib had slipped in the lower left chest, especially when the patient is bending forward. Ritvo[6] states that the most significant complaint is a feeling of weight or pressure under the xiphoid, coming on during or shortly after eating and relieved by a hot drink or by walking about for a few moments. Polley[3] concludes that there is no relation between the severity of symptoms and the type or size of the hernia, and Jones[20] is convinced of the importance of small hernias in causing pain.

Anterior Chest

The chest symptoms of hiatus hernia are frequently similar to those of heart disease, especially angina pectoris. Many observers (Harrington,[23] Dwyer,[17] Healy,[24] Truesdale,[25] Weitzen,[26] Johnson,[27] Jones[20] and Hedblom[28]) call attention to the importance of substernal pain in hiatus hernia, and to the fact that the pain may be agonizing and may radiate to the shoulder and down the left arm. Jones finds that substernal pain is more likely to occur in patients who have small hernias. He also mentions cases with substernal pain radiating to the left shoulder down the arm into the ring finger, and also points out that exertion, nervous tension and large meals are precipitating factors. Reid[29] describes a case of hiatus hernia occurring in a physician that simulated cardiac infarction. The detailed report of this case, with the various suggestions made by colleagues to explain the symptoms, is both interesting and instructive. In addition to substernal pain, many observers mention dyspnea and palpitation, especially in the recumbent position or after meals. Also, McGinn and Spear[30] describe a patient with a large diaphragmatic hernia who had a cor pulmonale and marked dyspnea. They suggest that compression of the lungs by the herniating stomach causes an acute right-sided heart strain.

Attempts to explain the cause of chest pain in hiatus hernia reveal some difference of opinion. Johnson[27] suggests that the cardiorespiratory symptoms are due to the pressure of the hernial contents on the vagus nerve as it passes through the hiatus. Gilbert, LeRoy and Fenn,[31] as a result of animal experimental work, found that distention of the stomach or peritoneal cavity caused a decrease in the blood flow through the circumflex branch of the left coronary artery, thus explaining attacks of angina pectoris in patients with distended stomachs. Jones,[20] in a careful study of the mechanism of pain in both angina and hiatus hernia, concludes that overdistention of the lower end of the esophagus or the herniated portion of the stomach, with or without associated esophagitis or gastritis, may be responsible for the production of anginal pain in any or all of its components.

Complications

It is generally agreed by various observers that hemorrhage is the most important complication of hiatus hernia. (Giffin,[4] Bock et al.,[15] Gardner,[32] Moersch,[18] Eusterman and Morlock,[33] Wilkinson and Adams,[34] Polley[3] and Jones.[20]) Concerning the actual cause of the bleeding there is some doubt. In a case reported in the Cabot Case Records,[35] bleeding was supposed to have been due to varices in the blood vessels of the gastric mucosa. Also, Bock concludes as a result of postmortem study that congestion of the mucous membrane of the stomach presumably caused by increased venous pressure is the cause of the bleeding. On the other hand, Truesdale, Hunt and Leigh[36] claim that hemorrhage is due to erosion or ulceration of a portion of the stomach that has become incarcerated, constricted or fixed. These authors also discussed the role of obstruction as a possible complication and, later, Truesdale[37] debated the problem of the development of gastric ulcer and possibly cancer. The possibility that large hernial sacs may cause right-sided heart failure has been mentioned previously.

* * *

The above review of certain articles from the literature is sufficient to demonstrate the fact that since 1912 there has been considerable interest in the subject of hiatus hernia, and that the symptomatology and differential diagnosis have been well described. However, if experience over a period of years in a large general hospital is any guide, clinicians have been slow to include this condition in the differential diagnosis of upper abdominal and anterior chest disease.

Since it has been possible to collect from the records of the Boston City Hospital a series of 128 cases during a period of less than four years, the condition is not rare. In fact, more attention to symptoms may demonstrate that the abnormality is fairly common.

Analysis of Cases

One hundred and thirty-six cases have been reviewed — 128 from the hospital records and 2 from the private files of one of us (W.R.O.). In the following tables an attempt is made to classify the various symptoms and signs, together with important complications.

Jones[20] classified as small those hernias that do not exceed a maximum diameter of 7 cm. In the hernias classified as large in his series, at least one third of the stomach was involved. Lacking definite information regarding measurements in our series, we have accepted the roentgenologist's description as and when given (Table 1), being careful to speak of large hernias only when at least one third of the stomach was herniated through the hiatus opening.

Table 1. *Size of Hernias.*

Size	No. of Cases
Small	58
Moderately large	12
Large (at least one third of the stomach herniated)	30
Unclassified	36
Total	136

Of the 136 patients with hiatus hernia, 18 were considered to have a congenitally short esophagus.

In the group of associated diagnoses (Table 2), there are a number of conditions that may give rise to symptoms similar to those of hiatus hernia.

Table 2. *Important Associated Diagnoses.*

Diagnosis	No. of Cases
Diverticulum of esophagus	3
Cancer of esophagus	2
Peptic ulcer	7
Cancer of stomach	4
Diverticulum of duodenum	4
Diverticulitis of colon	7
Gall-bladder disease: cholecystitis or cholelithiasis or both (diagnoses by x-ray or operation or both)	5
Total	32

Therefore, in the following discussion the 32 cases with important associated diagnoses are omitted, leaving a total of 104. The finding of 4 cases of diverticulum of the duodenum and 7 cases of diverticulitis of the colon is of some interest. Weintraub and Tuggle,[9] in a study of 310 cases of duodenal diverticulum, found that 9 per cent of the patients had an associated hiatus hernia and 23 per cent an associated diverticulitis of the large bowel.

In general, symptoms fall into groups suggesting peptic ulcer, gastrointestinal malignancy, gall-bladder disease or heart disease. Realizing that an absolute differentiation cannot be made, the best we can do is to group material according to predominant symptoms (Table 3).

Of the 9 patients without symptoms, 4 had small hernias and 5 had large hernias, with eventration of at least two thirds of the stomach.

Table 3. *Classification according to Predominant Symptoms.*

Symptoms	No. of Cases
Gastrointestinal	59
Gall-bladder	23
Coronary	13
None	9
Total	104

Among the thirteen cases with symptoms suggesting coronary disease, one or more of the observers who saw these patients was of the opinion that 6 of the patients had definite coronary-artery disease in addition to a hiatus hernia, and in one case this opinion was supported by suggestive electrocardiographic changes. Finally, it should be mentioned that in the 82 cases with symptoms suggesting either gall-bladder or gastrointestinal disease, careful x-ray studies revealed no disease other than a hiatus hernia. Despite this fact, several patients in this group were unnecessarily submitted to surgery.

Table 4 lists the symptoms in 95 cases, regardless of the size of the hernia. An attempt was made to classify symptoms according to the size of the lesion but without clear-cut differential data. It is to be remembered that hernial size may change from time to time and that a single observation by x-ray is not necessarily an accurate basis for a definite classification. At any rate, in the 13 cases with symptoms suggesting coronary disease, 5 patients had large, 2 moderately large, and 6 small hernias.

Table 4. *Distribution of Symptoms (95 Cases).*

Symptoms		No. of Cases
Epigastric pain or distress (shortly after meals, generally associated with sense of fullness)		55
Radiation to mid-back	4	
Radiation to shoulders	5	
Nausea or vomiting, or both		44
Heartburn		22
Belching		21
Night pain		16
Difficulty in swallowing		14
Weight loss		18
Loss of appetite		12
Dyspnea		7
Hiccough		3
Substernal pain		24
To right of sternum	2	
To left of sternum	5	
Radiation to mid-back	5	
Radiation to left shoulder	4	
Radiation to left arm	1	
Increased by exertion	4	
Unrelated to exertion	5	

The symptoms in 95 cases were relieved as follows: by assuming the upright position, 13 cases; by the use of soda, 11 cases; by vomiting, 6 cases; by belching and by lying down, 3 cases each; and by defecation, 2 cases.

Among the 104 cases, there were 29 cases with mild hemorrhage, and 12 with gross bleeding. Only those cases are included that revealed an appreciable fall in hemoglobin level and red-cell count and at least a ++ guaiac test for occult blood in the stools. Cases listed as having had a gross hemorrhage include only those with a hemoglobin level of 50 per cent or lower. Consideration of hemorrhage in relation to the size of the hernia is of interest (Table 5). Of real importance, however, is the observation that bleeding of either mild or severe type is just as likely to occur regardless of the size of the hernia.

TABLE 5. *Hemorrhage in Relation to Size of Hernia.*

SIZE OF HERNIA	TOTAL NO. OF CASES	CASES WITH MILD HEMORRHAGE	CASES WITH GROSS HEMORRHAGE
Small	43	12	4
Moderately large	10	2	3
Large	27	9	1
Unclassified	24	6	4
Totals	104	29	12

SUMMARY OF CLINICAL DATA

The typical symptom of hiatus hernia may be described as a sense of epigastric pain, distress and fullness coming on shortly after or during meals. Frequently this symptom is associated with nausea, vomiting, regurgitation, belching or a sense of burning, but not infrequently these symptoms are independent. Often there is difficulty in swallowing solid food, lack of appetite and associated weight loss. Very frequently there is epigastric pain or distress appearing at night or when the patient is in the recumbent position, but in most cases this pain is relieved when the patient assumes the upright position. For the digestive symptoms mentioned above, change in position may bring relief, but just as frequently soda gives relief, and occasionally a patient complains of inability to raise gas. There is often substernal pain or dyspnea or both — generally but not always unrelated to exertion. The pain may present a type of radiation similar to that of angina pectoris, but just as frequently its radiation is atypical. Furthermore, the patient with hiatus hernia may bleed. The bleeding may be of mild degree, in which event it may well explain the finding of anemia characteristic of chronic blood loss, or the patient may have a hemorrhage sufficiently severe to endanger life. Finally, it appears from this study — although definite proof is lacking owing to insufficient data — that symptoms and complications are not related to the size of the hernia.

Such is a composite clinical picture of a patient with hiatus hernia as drawn from the records of the Boston City Hospital. In general, this picture corresponds with the many found in the medical literature.

X-RAY DIAGNOSIS

Since the manifestations of hiatus hernia are so variable and inconstant that clinical diagnosis is usually impossible, x-ray demonstration is necessary to establish the presence of the abnormality. In some patients routine x-ray studies of the esophagus and stomach suffice to outline the hernia. In the majority of cases, however, the lesion is very small or for other reasons difficult to visualize. In these cases it may require the utmost care on the part of the roentgenologist to prove the existence of the hernia.

In searching for an esophageal hiatus hernia, the x-ray examination should always begin with fluoroscopic observations without the opaque meal. A careful and thorough search is made for a gas-containing shadow lying at or slightly above the level of the diaphragm. This is of particular importance since in some cases the hernia reduces itself and disappears on ingestion of the opaque meal. Observations are first made with the patient breathing quietly, then in full inspiration and forced expiration. The frontal and oblique positions are used in the erect, prone and supine positions. Occasionally both gas and fluid are present within the herniated portion of the stomach, presenting a horizontal fluid level with an air bubble above the liquid.

When the opaque meal is administered, the fluoroscopic observations are best begun with the patient in the erect position. Each mouthful is carefully observed in its passage through the esophagus. The lower end of the esophagus may be tortuous and moderately dilated. Rarely, pressure of the hernia produces esophageal obstruction, with consequent dilatation. In patients with congenital shortening of the esophagus, the cardioesophageal junction is seen to be above the level of the diaphragm. The hernia in many cases fills partially or completely with the patient erect. However, it has been our experience that the great majority of hernias are not demonstrable in this position. Therefore, if the x-ray observations are carried out only with the patient upright, as is the case in some clinics, a large percentage of the lesions will not be visualized and the diagnosis will consequently be missed.

It is with the patient lying down that the hernia is most apt to be demonstrated and its size and shape best outlined. Deep, forced breathing, pressure on the abdomen, lowering the head of the table, filling the colon with barium or air, asking the patient to strain or cough — these or other maneuvers that tend to increase the intra-abdominal tension may be used to help visualize the hernia. Complete filling of the stomach with the barium meal is important. The patient must be observed in the prone, supine and oblique positions, no one position being optimum for all cases.

Although fluoroscopic observations usually serve better than x-ray films for the demonstration of the hernia, the latter should be made in every case. Occasionally the lesion is visualized only in the films and not during fluoroscopy. Spot films exposed during roentgenoscopy are now available in most clinics and are extremely helpful in the study of difficult cases. The hernia appears as a rounded or oval shadow in the posteromedial portion of the thoracic cavity just above the diaphragm. Rugal folds are demonstrable in the herniated portion of the stomach, extending through the esophageal orifice of the diaphragm. The size and shape of the hernia vary widely in different patients, and in the same patient at various times. Small lesions may be but a few millimeters in diameter; the largest may comprise half or more of the stomach. The hernia most commonly lies to the left of and anteriorly to the esophagus. With large hernias the esophagus may appear to be encircled by the herniated portion of the stomach. Cancer or ulcer may occur in the hernia or other parts of the stomach, and a careful search for other pathologic processes should be made in every case.

Treatment

Hiatus hernia may present no symptoms and therefore require no treatment. All observers are agreed that treatment is essentially medical, especially in patients with small lesions. A bland, high-vitamin diet, divided into four or six feedings, is desirable. Food should not be given before bedtime. Assumption of the upright position after eating or for a few minutes during the course of the meal is often helpful. In many cases sleeping at an angle of 45° has relieved distressing night symptoms. Various alkalies and antispasmodic drugs are frequently useful. Recently Levy and Duggan[38] have emphasized the psychic factor in the management of such cases. Surgery is indicated when medical measures fail to give relief, especially in patients having intractable pain or hemorrhagic tendencies. A large measure of relief may result from interruption of the left phrenic nerve. On the other hand, surgical repair offers a complete cure, and the surgical technic of the procedure has been well standardized.

In our series, 4 patients had phrenic-nerve interruption and 1 was operated on for repair of the hernia, in all cases because of attacks of severe epigastric pain. In the 4 cases in which the phrenic nerve was interrupted, relief was either partial or temporary. In the single case of hernia repair, relief was permanent.

Discussion

It is generally believed that hiatus hernia is congenital. It must follow that most patients have the condition for many years before exhibiting symptoms. Actually, in most cases, symptoms come at a period in life when one may expect the onset of symptoms of other conditions, all of which serve to complicate the study. The symptomatology and clinical findings of hiatus hernia are inconstant and variable, so that although the existence of the condition may be suspected by the clinician, it is usually impossible to make the diagnosis with certainty on the basis of the history and physical examination alone. Furthermore, many of the complaints in hiatus hernia are also present in other, commoner diseases. It is highly desirable, therefore, to establish a syndrome on which a definite diagnosis is tenable.

In obtaining detailed histories of a large series of cases, a group of symptoms that have been met in a small number of patients but that have proved extremely significant are the following: a feeling of fullness, pain or distress in the epigastrium or under the tip of the xiphoid, coming on with the ingestion of the first few mouthfuls of food. In some cases these symptoms are so severe that they necessitate the interruption of the meal. However, on leaving the table and walking about for a short time, the patient may experience a sudden disappearance of the complaints, often with a feeling of something dropping or giving way in the region of the lower sternum. He is then able to return and finish the meal in entire comfort. The explanation is doubtless that the food first ingested produces filling of the herniated portion of the stomach, with distortion, compression and complete or partial obstruction of the esophagus; on arising and moving about, the herniated portion of the stomach empties or reduces itself, with resultant disappearance of the symptoms. In the experience of one of us (M.R.), this is pathognomonic of hiatus hernia, and although it occurs in relatively few cases, permits a practically definite diagnosis. Rarely, patients with

cardiospasm or esophageal diverticulum may give a somewhat similar history. In these conditions, however, the relief is usually not produced by arising and walking about, nor is it so immediate and complete.

Inasmuch as the clinical picture of hiatus hernia is similar to that of other disease in the chest or abdomen, one must be entirely certain of the state of affairs before assuming that hiatus hernia is the only cause of existing trouble. Recently we have seen a case of hiatus hernia with severe gastrointestinal bleeding in which the first gastrointestinal x-ray examination revealed no disease other than the hernia. A repeated x-ray study, however, revealed a deep duodenal ulcer in addition to the hernia. The problem becomes all the more difficult when one tries to explain attacks of chest pain on this basis. Certainly a patient may have both coronary-artery disease and a hiatus hernia. It is only after very careful study and observation, therefore, that a single diagnosis is tenable. The possibility of hiatus hernia should never be forgotten, and its presence never overlooked. Nevertheless, in one's enthusiasm at finding an abnormality that can be demonstrated, one should not neglect the fact that other disease may be present the existence of which can be demonstrated only by continued study and observation.

Summary

Hiatus hernia is sufficiently common and the symptoms are such as to justify its inclusion in the differential diagnosis of anterior chest or upper abdominal complaints or both.

The presence of hiatus hernia should never be overlooked, regardless of its size.

In any case of unexplained bleeding, the presence of hiatus hernia should always be considered, since bleeding may occur in any type of case.

The symptoms of hiatus hernia may simulate those of coronary-artery disease. The differential diagnosis here is a matter of careful clinical judgment after all the data have been assembled.

A clinical syndrome pathognomonic for hiatus hernia has been suggested.

A method for determining the presence of hiatus hernia by roentgenologic examination is presented.

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PANEL DISCUSSION: CURRENT EPIDEMIC RESPIRATORY DISEASES IN CHILDREN*

CHAIRMAN'S INTRODUCTORY REMARKS

DR. CHESTER S. KEEFER, Boston: I need not tell an audience of this kind that the respiratory infections are by far the most important group of illnesses that we deal with in medical practice. One sees them every day, and they always raise important and frequently distressing problems. We know that the respiratory infections are responsible for more disabling illness, for more absenteeism from school and from industry, than any other single group of disorders. Dr. Sisson has already referred to the fact that great strides have been made in treatment in the last few years, but very few advances have been made in prevention. So tonight the speakers are going to confine their remarks, in the main, to the treatment of these respiratory infections that are encountered every day.

ACUTE LARYNGOTRACHEO-BRONCHITIS IN CHILDREN

JOHN A. V. DAVIES, M.D.†

BOSTON

I HAVE been asked to discuss what may safely be called a pediatric emergency. As you know, in past years acute laryngotracheobronchitis has carried a mortality of anywhere from 50 to 100 per cent.

When a physician is called in the dead of the night by a mother who says her infant has croup, the chances are that he has croup, and probably one is justified, after questioning her, in telling her to put the child in a room with warm steam and to give some suitable expectorant. However, it is important to bear in mind at the very outset that what seems to be a simple case of croup may actually be the start of something far more serious, that is, acute laryngotracheobronchitis.

One other disease that we see infrequently nowadays, diphtheria, should of course be borne in mind at the same time. But spasmodic croup usually follows a mild respiratory illness, most often begins at night, after perhaps a day out in the cold air, and as a rule quickly responds to steam and suitable doses of ipecac. The mother should be warned that if the child does not respond in one or two hours, she should notify you at once, and you should examine the child carefully.

At the outset, it is often difficult to differentiate these conditions. However, acute laryngotracheobronchitis may usually be distinguished from simpler and milder forms of respiratory illness by the fact that the symptoms are progressive and persistent. The child seems sicker. There is fever, and leukocytosis also. Therefore, if the symptoms do not respond quickly to steam and an expectorant, it is obvious that additional measures should be taken to deal with this threatening situation, and there is no doubt that the hospital is the place for such a child.

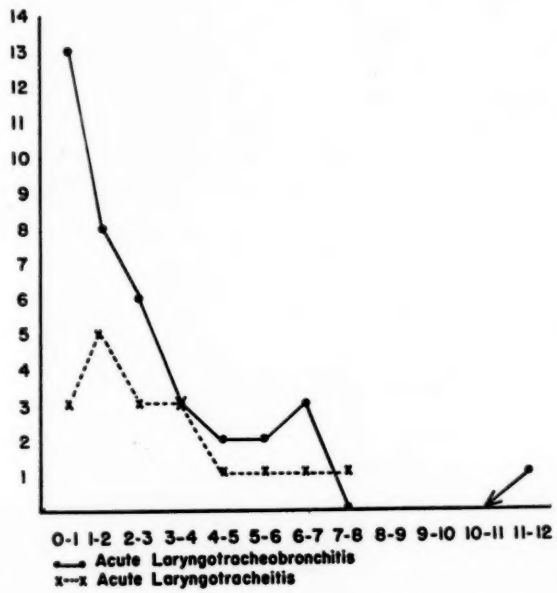

FIGURE 1. *Age Incidence in 38 Cases of Laryngotracheobronchitis and 18 Cases of Laryngotracheitis. Of the former patients, 21, and of the latter, 8 were under two years of age.*

Before speaking more specifically of therapy, I should like to remind you of the pathology of the disease. One is not dealing with a simple laryngitis, nor with a simple tracheal irritation. As the name implies, the inflammation extends from the throat down to the bronchi, and possibly to the bronchioles. In the early stage of the

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disease, one encounters inflammation and marked swelling of all these tissues, so that the airway is restricted. Later on, if the disease progresses, and especially if certain organisms of which I shall speak in a moment are present, necrosis and sloughing of the membrane and plugging of the bronchi may develop with resultant atelectasis and emphysema, and possibly pneumonia. The process is widespread, and no one portion of the respiratory tract is involved.

TABLE 1. *Bacteria Recovered on Repeated Cultures in 33 of 38 Cases of Laryngotracheobronchitis.*

ORGANISM	NO. OF CASES	PER CENT
Pure cultures	15	45
Beta-hemolytic streptococcus	8	24
Staph. aureus	4	12
Pneumococcus	3	9
Mixed cultures:		
Above organisms (various combinations) and *H. influenzae*	12	37
Negative cultures	6	18

Figure 1* will remind you of the age incidence of this disease, showing that in the majority of cases the disease occurs during the first two years. Indeed, almost 50 per cent of the patients are two years of age and under.

Table 1 shows the bacteria that invade the respiratory tract. I show this because there has been a tendency to consider the beta-hemolytic streptococcus as the only organism involved, whereas *Staphylococcus aureus* and the pneumococcus are also frequently present, as well as *Haemophilus influenzae*. Table 2 is even more illuminating. In patients under two years of age, the staphylococcus is more frequently found in pure culture than is the streptococcus; after that, the streptococcus appears more important. From Table 3 it is apparent that among the autopsied cases *Staph. aureus* was also important, and that in all the fatal cases the children were under two years of age. The streptococcus and the pneumococcus were also recovered, but the staphylococcus appeared in every case, — except one in which only a throat culture was taken, — not only in the trachea and the lungs but also in the blood stream. I have emphasized the bacteriology because the tendency nowadays is to treat specific organisms in a specific way.

Standard treatment at the Children's Hospital involves teamwork between the physicians, the nursing staff and the laboratory. We have decided that the hot steam room is not so good as a room in which we have a cold humidifier and in which the temperature is kept at a level of approximately 70 to 75°F. We think that the hot room is uncomfortable to the patient and to the attendant as well. We avoid unnecessary examinations and treatments. However, we believe that it is important, having placed a child in this humidified room, to obtain the proper cultures from the throat or trachea. We also like to get a blood culture, because now and then the invading organisms are more clearly identified by this method. However, undue measures are not taken to obtain these cultures, especially when the child is precariously near the borderline between life and death. From this point on, the procedure is largely a matter of the skill and judgment of the attending physician.

TABLE 2. *Bacteriology in Cases of Laryngotracheobronchitis according to Age.*

ORGANISM	UNDER 2 YEARS			OVER 2 YEARS			ALL CASES	
	PURE CULTURE	MIXED CULTURE	TOTAL	PURE CULTURE	MIXED CULTURE	TOTAL	NO.	PER CENT
Beta-hemolytic streptococcus	2	5	7	6	2	8	15	45
Staph. aureus	4	10	14	0	1	1	15	45
Pneumococcus	1	4	5	2	0	2	7	21
H. influenzae	0	3	3	0	1	1	4	12

On the way to the hospital, if an ambulance is employed, it is well to make sure that one has some oxygen at hand. In case the child's airway becomes completely blocked off, which sometimes happens when a child is taken from the warm home out into the winter air, a life may be saved if the accompanying physician inserts a Mosher tube into the trachea.

Having made the decision to bring the child to the hospital, it is important to put a capable laryngologist on the alert and tell him he may be called to do something for the child. What he does depends a good deal on his experience and the progress of the patient. From observation of the course of events at the Children's Hospital, I believe that in most cases tracheotomy is probably the operation of choice, if operation is necessary. It usually provides permanent relief from high obstruction. It enables one to insert a catheter and aspirate the pus and some of the exudate from the upper bronchi and lower trachea.

*For Figure 1 and Tables 1, 2 and 3 I am indebted to Dr. Charles H. Cutler and Dr. Charles F. Ferguson.

On the other hand, the intubation tube tends to cause necrosis of the larynx and trachea and is sometimes coughed out, leaving the child in the condition in which he began.

I emphasized the bacteriology of the disease because we now have the assistance of the sulfonamides and penicillin. Since one is dealing with different organisms, not exclusively with the streptococcus, sulfathiazole or sulfadiazine may well be started on the way to the hospital. At present, penicillin is not available for general use. The dosage of the sulfonamides will be discussed later, but it should be emphasized that a full dose should be given early.

TABLE 3. *Bacteriology of Fatal Cases.*

Case No.	Age	Organisms	Source	Day of Illness Cultured	Remarks
	mo.				
19	15	Pneumococcus (Type 23) and *Staph. aureus*	Trachea and lung*	1	
		Pneumococcus (Type 23)	Blood*	1	
21	12	Beta-hemolytic streptococcus	Throat	3	No autopsy
25	12	*Staph. aureus*	Trachea	2	
		Staph. aureus	Trachea	3	
		Staph. aureus	Trachea, lung and blood*	4	
28	19	*Staph. aureus*	Trachea	1	No autopsy
30	10	Pneumococcus and *Staph. aureus*	Throat	2	
		Staph. aureus	Bronchus, lung and blood*	4	
36	14	*Staph. aureus*	Throat	2	
		Staph. aureus and pneumococcus (Type 23)	Trachea	2	
		Staph. aureus	Trachea and blood*	3	
38	12	*Staph. aureus*	Trachea	2	No autopsy
		Beta-hemolytic streptococcus	Trachea	9	
		Beta-hemolytic streptococcus	Trachea	14	
45	13	Beta-hemolytic streptococcus	Throat	2	No autopsy
		Staph. aureus	Trachea	3	
50	15	Beta-hemolytic streptococcus	Larynx	2	
		Beta-hemolytic streptococcus and *Staph. aureus*	Blood*	5	

*Cultured at autopsy.

Oxygen administration is probably elective in some cases, although it should be used when cyanosis is present. It may be necessary to give it by nasal catheter. If infants under two years of age do not respond in a reasonable time to sulfonamide therapy and general supportive measures, a transfusion of blood from an adult donor should be considered, in the hope of providing certain unknown factors that the infant does not have and that some adult may possess. Transfusions seem to help some infants with staphylococcal infections.

The question arises whether one should give other drugs, such as ipecac. I should say, No. Morphine and atropine are absolutely contraindicated, since morphine suppresses the respiratory effort, and atropine dries the secretions, already too tenacious, and thus tends to plug off the respiratory tract.

A last point concerns fluids. We try to give fluids in moderate amounts, by mouth, even after tracheotomy. If the child's condition is too bad, we give them subcutaneously. It is important, however, to remember that in a situation like this one should avoid flooding the patient with fluids because the respiratory tract is already seriously embarrassed and adding a great deal of fluid to the circulation may increase the edema fluid in the bronchi and bronchioles and cancel all that has been gained by the previous treatment.

THE DIAGNOSIS OF VIRUS AND BACTERIAL PNEUMONIA IN CHILDREN

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BOSTON

THE TERM usually applied to acute infection of the lung, other than lobar pneumonia, is "atypical pneumonia." If I were to enumerate the various terms that have been introduced in recent years as synonyms for or forms of atypical pneumonia, my time would be up before I finished. In general, the term "virus pneumonia" is loosely used to express the desire of the physician to approach an etiologic diagnosis that he cannot make.

I shall mention briefly some of the problems involved before one can rule out a definite etiologic agent, and then some of the known agents other than bacteria that may cause pneumonia. This will still leave a residue, which is bothering most of us more, perhaps, than those cases in which the etiology can be determined.

In the first place, atypical pneumonias are the ones predominating among infants, even when the causative organism is one which in older people produces lobar pneumonia, namely the pneumococcus. All other organisms produce atypical pneumonias, even in adults. Thus we have atypical pneumonias due to all bacterial agents in infants, and to all bacterial agents other than pneumococcus in young children, in whom the pneumococcus produces typical lobar consolidation.

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Pediatricians are only too well aware of the difficulties in arriving at an etiologic diagnosis in infants. First is the problem of obtaining proper materials for culture. Then again, multiple organisms are usually isolated from the nasopharynx or sputum in infants, and one is confronted with the difficulty of arriving at a conclusion concerning which of the organisms is actually causing the disease. Nowadays, the direct observations afforded by the Neufeld typing of pneumococci are of great assistance. Cultures of the material that is aspirated or is taken on a swab after encouraging a child to cough can frequently give a predominant organism, and this can usually be considered as the etiologic agent. Blood cultures are most helpful in bacterial infections.

It must be remembered that besides the pneumococcus, the staphylococcus is an important etiologic agent, especially in infants, in whom aspiration of upper respiratory contents is an important factor. The streptococcus is one of the foremost causes of the pneumonias that follow virus infections, such as measles. It is also found in the pneumonias that occur after whooping cough, and after other streptococcal infections, like scarlet fever, tonsillitis and septic sore throat.

The pneumonia produced by the streptococcus is characterized in infants and in young children by a severe type of illness that advances rapidly and is accompanied by a rapid accumulation of fluid in the chest and by extreme toxemia.

Staphylococcal infection of the lung is characterized by an insidious onset of a severe illness. There is a purulent or perhaps pinkish sputum representing an admixture of pus and blood. There is usually a severe tracheobronchitis. The course of the disease is characterized by multiple cavities in the lung, and the tendency in young children to produce abscesses that rupture into the pleura, giving rise to pyopneumothorax. Staphylococcal pneumonias occur most frequently after influenza or following aspiration in debilitated infants and children.

The influenza bacillus may cause severe infections in the lung, particularly during epidemics of clinical influenza. It is also characterized by a lesion in the trachea and bronchi and by a hemorrhagic type of bronchopneumonia that is sometimes seen in the fulminating form of a staphylococcal pneumonia.

In infants, the factor of inhalation of foreign substances, including their own upper-respiratory secretions, is important in establishing lesions in the lower respiratory tract. Foreign bodies producing or predisposing to severe and recurrent pneumonias must always be borne in mind. Any of the common pyogenic bacteria can cause pneumonia under proper circumstances.

Of the nonbacterial agents, the commonest is the virus of influenza, which is capable of producing various lesions in the lung. It may also predispose to severe bacterial infections, particularly with the staphylococcus or influenza bacillus, and sometimes with other organisms, such as the streptococcus. The latter is likely to produce the post-influenzal pneumonias if streptococcal infection happens to be prevalent, or in wards where streptococcal infections occur. The pneumonia would then be characteristic of the streptococcal type.

The psittacosis virus produces a disease in human beings almost exclusively after contact with exotic birds. Recently a good deal of attention has been focused on this virus and other closely related viruses that occur in many species of birds, including certain domestic birds, such as street pigeons and domestic fowl. The disease caused by these viruses is termed "ornithosis." These agents are extremely interesting and have other relatives in the virus family, many of which, under certain circumstances, may produce pulmonary lesions and others of which are not known to produce pulmonary lesions. The diagnosis of psittacosis or ornithosis in the absence of a history of definite contact with birds is difficult. Even with such a history the diagnosis is sometimes questionable, because of the wide variety of strains that can give immunologic reactions with these related viruses.

A number of other viruses have been isolated from cases of atypical pneumonia, mostly in adults. Presumably similar cases occur in infants and young children, since there are many reports of their occurrence in small outbreaks among adolescents. One group of these viruses produces pneumonia and meningitis in mice and has been called "meningopneumonitis." Another virus has been isolated by inoculating material from human beings into cotton rats. Still another virus can be isolated only by inoculation of the mongoose, a rodent that is native to Jamaica and is not available in this country.

There are many other viruses, one of which occurs in mice, that are also closely related to the viruses of psittacosis and meningopneumonitis. A virus has been recently described that has been transmitted from kittens to human beings; this virus produces a characteristic pneumonia in young kittens, but not in adult cats.

There are other possibilities. There is Q fever, which in America has been shown to be the cause of endemic cases as well as small outbreaks of pneumonia. In Australia the agent of Q fever

produces a disease simulating influenza, and it has not been recognized as producing pneumonia there. The agent is presumably identical with that of American Q fever; both are rickettsias.

In addition to these viruses, there are others that may also be associated with lesions in the lung, presumably due to these nonbacterial agents. For example, epidemic typhus fever and South African tick fever are known to give pulmonary lesions that are similar to the pneumonias produced by other viruses. Lymphocytic choriomeningitis may also do this.

The important point is that after one tries to identify the etiologic agent with all those I have mentioned, one has identified only a small proportion of the pneumonias that are not due to bacteria. In general, the recent tendency has been to make a diagnosis of virus pneumonia when a person has been treated with a sulfonamide drug and fails to respond to it. However, one must remember two things. In the first place, even the common bacteria that are known to respond are sometimes resistant to the action of sulfonamide drugs. This is occasionally true of the pneumococcus, but resistance of pneumococcal pneumonia to sulfonamide therapy cannot be said to be a common phenomenon. Secondly, it is to be remembered that pneumonia due to organisms like the streptococcus and staphylococcus requires prolonged and intensive treatment. Thus, if one starts out with a mild infection that one is trying to treat with small doses, and the patient becomes suddenly severely ill, one may assume that one is dealing with a virus pneumonia that has not responded, when actually one is dealing with a severe staphylococcal or streptococcal pneumonia that has been inadequately treated.

There are other diseases, particularly of infants, that are suspected of being of virus etiology owing to the pathological picture. There was an epidemic disease among the newborn in Minnesota in which intracellular inclusions have been demonstrated both in the lung specimens and in materials obtained from the throat. It is also true that if one examines the lungs of children who die of whooping cough, a large percentage of them have intranuclear inclusions in the epithelium of the bronchi. What relation these inclusion bodies have to the etiology of whooping cough on the one hand, or to the pneumonia of which the infants die on the other, is not altogether clear.

There are other conditions from which infants die, as, for example, malnutrition and other debilitating diseases, in which intracellular or intranuclear inclusions, or both, are found at autopsy. The relation to the fatal illness or to the pneumonia that may be present is difficult to evaluate in such cases.

THE USE OF SULFONAMIDES IN THE TREATMENT OF RESPIRATORY INFECTIONS IN CHILDREN

CHARLES A. JANEWAY, M.D.*

BOSTON

THE chemotherapy of the common respiratory diseases of children presents many difficulties that one does not encounter in dealing with adults. One hears quite frequently somewhat intolerant remarks concerning practitioners who use sulfonamide drugs indiscriminately. I think that all those who do much work with the sulfonamides feel strongly against the indiscriminate use of the drugs, but in my brief few months in pediatrics, I can sympathize most heartily with those whose job it is to see children in the home and to decide with what types of infection they are dealing.

The last speaker, who probably knows as much about this subject as anyone in the field, has shown us how complex the problem has become. The job of the person seeing a sick child in weeding out the various etiologic agents is often extremely difficult, and one can hardly blame doctors for using these drugs almost indiscriminately, since in many cases they are effective. However, I consider that a defeatist attitude, and one that should not be encouraged, because there are definite indications and contraindications for their use. Children and adults got well before the days of chemotherapy. One should not let enthusiasm for a new therapeutic agent run away with one every time a person becomes ill.

What are the indications? They boil down to evidence of an acute bacterial infection of the respiratory tract that is obviously spreading and is a serious or potentially serious one.

We know that respiratory infections are due to two types of agents in general, and frequently the two agents act together. On the one hand are the viruses; on the other are the bacteria. One can make a fairly good generalization of the respiratory diseases, namely, that the sulfonamides are fairly effective against almost all the bacteria that cause respiratory infections, with the possible exception of the staphylococcus. Nevertheless, they are singularly ineffective against the virus agents that often pave the way for the bacterial infections, or may be the sole cause of the infection.

Therefore, anyone using the sulfonamides should try to bear in mind this question, What are the bacterial infections of the respiratory tract? And this, also, should be borne in mind: If the child shows by his clinical picture that he is suffering from a bacterial infection, how serious is that

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infection? For every bacterial infection does not need to be treated with a sulfonamide: only those that are actually serious or potentially serious require it.

What signs does one have? Perhaps the first that is of considerable help is gained by just looking at the child. How sick is the child? For example, an ordinary cold may make a child extremely uncomfortable. He may have an obstructed nose, or a cough and he may be hoarse and have a little croup; but he is not apt to have a temperature of 104 or 105°F. and be prostrated, with a marked diarrhea, vomiting or other signs of general toxicity. One cannot get away from the fact that the person who can use the sulfonamides wisely is the best doctor. One cannot lay down rules for the use of these therapeutic agents that will work for an automaton. One has to use judgment. Therefore, the first question is, How sick, really, is the child? Secondly, are there any signs of invasion? Bacteria that are localized are no great menace. It is the bacterial infection that spreads that menaces the child.

The spread in the respiratory tract is easily seen. The infection first spreads to the sinuses, which become tender and fail to transilluminate. Then there are the ears, the commonest site of all. The patient develops an acute otitis media, possibly with swelling of the mastoid process, and mastoid tenderness. A site equally common is that of the lymph nodes that drain the area. If these become swollen and tender and increase visibly in size, obviously there is an infection spreading beyond the ordinary bounds of the upper respiratory tract. The lungs, again, are a site of spreading infection. However, as already pointed out, invasion of the lungs may be purely of a virus nature.

Regarding general signs, fever, general toxicity and leukocytosis are gauges both of the severity of the illness and at times of its nature. Unfortunately children, as I have learned to my distress in the last few months, do strange things, whereas adults react more regularly. As a generalization, to which many exceptions may be taken, the virus infections of the respiratory tract are accompanied by a real leukopenia. The white-cell count, in the face of a fever, fails to go up, and even goes down. On the other hand, bacterial infection may produce a queer reaction in the bone marrow, associated with a fall in the white-cell count instead of the usual rise, which when present is a helpful sign of bacterial infection.

Having considered all these things, one admits that the child is very sick but does not know what is the matter with him, except that he has an infection of the respiratory tract. He has a cough and the eardrums are a little injected; the throat is red, and the temperature is 104°F.; he is prostrated, vomiting and refusing food, and he is fussy. I think that under those circumstances anyone would be foolish to suppose that he runs a greater risk by giving the child the sulfonamides than by failing to do so. My own philosophy is to take the bull by the horns. If I were worried about the patient, I should go ahead and give the sulfonamides a trial. In about two or three days one will be able to determine whether any effect has been produced. If one undertakes to give the child a trial of chemotherapy, he should be sure to give the child enough drug so that it will mean something. Chemotherapy should, in my belief, either be fairly intensive or should not be employed at all. A little chemotherapy for a doubtful situation is one of the worst abuses to which the sulfonamides have been subjected. It does the patient no good and the physician is up in the air at the end of three days, not knowing whether the child is sick from the sulfonamides or from the infection, or whether the sulfonamides have done him any good. He is about three days worse off than before he started.

What are the complications associated with the use of the sulfonamides? First, there are the toxic reactions to the drug, for which the child has to be watched closely. Secondly, there is the possibility that the child may become sensitized and thus will be in for trouble when he subsequently needs the drug for a much more serious infection in the future.

What does one have to watch in the child to whom one gives chemotherapy? If it is given fairly intensively and early, and as soon as the infection is brought into control the dosage is lowered, the toxic reactions one has to fear most are those involving the kidneys. A child's urine should be examined for the presence of red cells, indicating damage to the kidneys, and the mother should be instructed to try to get some idea of how frequently the child is voiding. The blood has to be watched to a certain extent. Hemolytic reactions are rare with the new sulfonamides. Depression of the bone marrow with agranulocytosis usually does not develop until after ten to fourteen days of chemotherapy. Sensitization with fever and rash is most apt to occur in the second week. One's idea should be to treat the child intensively in the beginning, and get him off chemotherapy, if possible, before serious toxic reactions are likely to occur.

What should be done before chemotherapy is started? I should like to re-emphasize the fact that, although cultures are not always possible in the home, bacteriologic study of infections is just

as much a part of the study of the infected child as listening to the chest or looking down the throat. Certainly, in any seriously ill child or adult, the best cultures that can be obtained should be taken before chemotherapy is instituted, not because it may be impossible to get positive cultures after several days of therapy, but because by that time it may be important to know in a short space of time what the infecting organism is. If one has to wait twenty-four hours for the laboratory report, when a child is desperately ill, a fatality may result. Knowing what type of infection is present puts one in a relatively strong position. One has all the facts, as best he can get them. The cultures may not be too satisfactory, but at least one has made an effort. The blood culture in any seriously sick, hospitalized child should be taken, if it is humanly possible.

What drugs can be used? Obviously, sulfadiazine is the most satisfactory of the sulfonamide drugs; it disturbs the child, as well as adults, much less in every way. Its sodium salt can be given parenterally with great ease, and therefore is the ideal drug. However, one might as well be forewarned. It may not be possible to buy sulfadiazine much longer — it is just one of the shortages, like butter and coffee, that we may have to get used to. It should be remembered that all the infections that respond to sulfadiazine respond to sulfathiazole. It is my practice in urinary-tract infections, which are out of the field of this discussion, to use sulfathiazole. That means that one does not use sulfadiazine for everything, and thus can save it for the serious conditions, which are usually the respiratory diseases.

Sulfathiazole can be used in the same doses as sulfadiazine, with the single exception that one must remember that sulfathiazole is much more rapidly excreted, and thus it is more difficult to maintain an adequate concentration in the child by its parenteral use without getting renal complications.

Finally, there is the question of how much to give. I should like to re-emphasize a single point: do not give chemotherapy until you have made up your mind, on the basis of what you see, whether or not the child has a severe infection. If so, use it. And use enough. That does not mean too much. We have had the pendulum swing both ways. First, people gave too little; then they began to use such large doses that many children developed toxic reactions. One has to remember that the kidneys are the site at which sulfathiazole and sulfadiazine can produce their immediate and early toxic effects. It is especially true of children that when they have a severe infection, they may be quite dehydrated. It is dangerous to push too large doses into dehydrated children without being sure that adequate fluid is administered to maintain a good flow of urine.

The dosage in general, if one goes by rule of thumb, is approximately 1 gr. per pound for the first twenty-four hours in any serious infection. If a child is seriously ill, one half to three quarters of this amount is given as an initial dose. If a child has pneumonia, the initial dose is ¾ gr. per pound, and then 1 gr. per day per pound divided into four or six doses, whichever is most convenient. A day or two after the child's temperature comes down to normal, this can be cut down to ½ gr. per day per pound, and kept up a few days more until the infection is obviously well under control.

Sodium sulfadiazine can be given in 5 per cent solution by clysis under the skin, and, because it can be used in such concentrated solution, may be administered by syringe quite readily. In a severe infection, where vomiting is present, this has been satisfactory. These drugs cannot be given satisfactorily by rectum. With sodium sulfathiazole, 2 per cent is as high a concentration as I should want to use under the skin.

Discussion

Dr. Keefer: Dr. Davies spoke about the treatment of acute laryngotracheal bronchitis. He told us that it is a disease that frequently starts abruptly, is seen most frequently in children under the age of two years and is associated with a variety of organisms, including hemolytic streptococcus, staphylococcus and pneumococcus. He also told us that one should not use morphine or atropine in the treatment of these patients. He emphasized the importance of a humidified room with a temperature of 70 to 75°F. He was not in favor of cold outside air. In treatment, he advises the use of the sulfonamides and oxygen and, in some cases, tracheotomy.

The first question that has been submitted has been answered in large part by Dr. Davies in his discussion. It is as follows: "Discuss the treatment of acute laryngotracheal bronchitis, with reference to the effectiveness of croup tents and steam inhalations, to the influence of cold, outdoor air and to the use of the sulfonamides. What are the criteria for tracheotomy and for intubation?" I should like to have him define more clearly the criteria for tracheotomy.

Dr. Davies: That is not an easy question for me to answer, since I am not a laryngologist. However, although intubation is still favored by some in this country, the trend is definitely toward tracheotomy, if some measure of this sort must be undertaken. The laryngologists tell me that the trend is also toward medical treatment and away from surgical treatment. That is, the child is put at rest in a humidified room, sulfonamides are administered and, in general, supportive measures are given. When that is well done, it is possible to cut down the number of children who require tracheotomy.

One difficulty with intubation is that the tube sometimes cannot be inserted without considerable trauma to

the swollen tissues. As the child breathes and coughs, there is constant motion of the tube, which tends to cause necrosis and ulceration of the mucous membrane, with subsequent scar formation. Occasionally an operation is required to remove the tube.

Indications for tracheotomy itself are not always easy to define. Certain things must be borne in mind. One should not be guided by the child's voice. Some children have unaffected voices, and yet they may be in severe distress. One should be guided most of all by the general condition of the patient. How restless is the child? How cyanotic or fatigued is he? If the disease progresses and the child becomes weaker and weaker, a point may be reached where the child actually seems to relax. To the untutored eye, the patient may seem better. However, this change is a great pitfall, because actually it may be the stage before the end. Therefore, it requires some experience and considerable judgment to decide when tracheotomy should be done. In general, it should not be postponed until the child is completely exhausted, because death may occur quickly.

Tracheotomy, of course, is not without hazards. When it is done, the child usually gets considerable relief. It also enables one to insert a catheter and remove some of the secretions in the upper bronchi. I might add that now and then the bronchoscope is useful in removing thick crusts and secretions that plug the bronchi. In the presence of atelectasis, bronchoscopy may be advisable to relieve the obstruction.

DR. KEEFER: The next question is for Dr. Finland: "What is your opinion concerning the use of convalescent serum in the treatment of virus pneumonia?"

DR. FINLAND: That is a difficult question, and there is very little experience on which to base the answer. I might say first of all that there is no precedent to indicate that one might expect a good result from the use of convalescent serum, even if it is assumed that a virus is the etiologic agent. To my knowledge, there has not yet been demonstrated, either experimentally or clinically, any disease in which a cure has been accomplished by the use of the immune serum in a virus infection *after the infection has become established.*

I am certain that if there is anyone here who has seen a patient recover after receiving such convalescent serum, especially in large amounts, he would assume that the recovery was related to serum administration, and I suppose that in a single case that might be true. There is, of course, the possibility of modifying the disease, such as is supposed to occur in measles, and this cannot be excluded in virus pneumonia. However, I think one thing should be said: if convalescent serum is given, general experience with other infections indicates that fairly large amounts should be used. It would be interesting to find out whether such infections do respond. I hope that this will be tried under well-controlled conditions, and that it will yield some useful results.

DR. KEEFER: The next question is for Dr. Janeway: "How common are serious blood and kidney reactions with small doses of sulfadiazine, small doses being defined as ½ gr. per pound or less given for less than four days?"

DR. JANEWAY: I have answered this question indirectly before. I do not believe that anyone ought to begin treating a patient with an infection, except one in the urinary tract, with a dose of that size. Therefore, this should not happen. However, one may say that serious kidney reactions would probably be rare with a dose of less than ½ gr. per pound per day.

Serious blood reactions, as I pointed out before, practically only occur after a period of ten days of chemotherapy. The size of the dose doubtless has some influence on whether a patient develops agranulocytosis. This is certainly commoner with large doses than with small ones. But I do not believe that the dose is the whole factor, by any means. I might toss the ball to Dr. Finland, who is much more experienced than I am. Do you think agranulocytosis is much less apt to occur with small doses, provided they are carried over a long period of time?

DR. FINLAND: I do not know whether it is more or less frequent, but it certainly does occur with small doses.

DR. KEEFER: I am going to give the next question to Dr. Davies: "Should sulfadiazine be given to every case of acute otitis media?"

DR. DAVIES: That is a hard question to answer. The practitioner who first sees the patient in the home has the most difficult choice and decision to make. In the first place, one is not always treating just the acute otitis. Furthermore, the age of the patient makes a great deal of difference. Very often the past history enters into the picture. If a child has been subject to repeated infections of the upper respiratory tract,—sinuses and so on,—one should be more ready to use the sulfonamides in the early stages of acute otitis media than in a child who, up to that time, has been in robust health.

I am sure that the general appearance of the nose and throat makes a difference. A child with large, bulky adenoids, a postnasal purulent discharge and possibly with swollen tonsils may require the early use of the sulfonamides.

Then there is the appearance of the ear itself. We are all familiar with the child who has had a mild cold and awakens at night with earache. What steps should be taken beyond the use of nose drops? If, in addition to the other considerations, the ear itself is acutely inflamed and bulges markedly, even though one may be dealing with a simple catarrhal condition, I am in favor of opening the ear and using sulfathiazole or sulfadiazine, taking a culture at the time the ear is opened.

The number of cases of mastoiditis seen nowadays is much less than formerly, and it is difficult to escape the conclusion that in some measure the reduced incidence is due to the wider use, in selected cases, of sulfonamides.

DR. KEEFER: The next question goes to Dr. Finland: "Will you discuss briefly the parenteral use of sulfonamides, the indications, the route of administration, the concentration and the question whether or not alkalies should be given along with sulfonamide treatment?"

DR. FINLAND: This subject has been covered by Dr. Janeway, but there are a few points worth emphasizing. The most important point I should like to drive home is that, whereas in general one should faithfully follow the instructions that come with the packages in which drugs are contained, because the instructions are usually approved by the Food and Drug Administration and also by the Council on Pharmacy and Chemistry of the Amer-

ican Medical Association, this is one exception. The Food and Drug Administration does not permit anyone to include in the literature directions for the use of sulfonamide drugs by the parenteral method, except as a sodium salt, given as a 5 per cent solution in distilled water. We used it once or twice that way, but we certainly have not adopted this method as a routine. We almost always give it in physiologic saline solution, chiefly because it is more convenient.

Several points concerning parenteral therapy should be emphasized: It should never be given in the same apparatus or together with blood, because clots may form when the sodium salts are mixed with whole or citrated blood. If one uses glucose solution, one should never permit it to boil in the presence of the drug, because the glucose inactivates the drug by combining with it to form a compound that is inactive when given parenterally. If given in distilled water, intravenously, it should be given only in a 5 per cent solution. In infants or in adults where it is not possible, not feasible or not convenient to use the intravenous route, or when intravenous injections are undesirable, the subcutaneous and intramuscular routes may be used.

British and Canadian physicians resort to the intramuscular use of high concentrations of the drug. There one has to use distilled water because the drug is not so soluble in saline as in distilled water. Most of the sodium salts are not soluble in saline in more than 2 or 3 per cent concentration; at least, they do not stay in the solution very long. The British originally used sodium sulfapyridine in a 33⅓ per cent solution intramuscularly and noted few complications, although sloughs did occur, particularly when some of the material escaped in the subcutaneous tissues. Fewer complications have been noted with the sodium salts of other drugs than with that of sulfapyridine, but in general the intramuscular use of the high concentrations is not desirable, because of the possibility that high concentrations will get into the subcutaneous tissue and produce irritation. Since the sulfonamides are usually given parenterally to the sickest patients, who have frequently lost a good deal of fluid by sweating and vomiting, and who have had difficulty in taking adequate amounts of fluid by mouth, we like to use the drug in smaller concentrations — namely, in 0.5 or 1.0 per cent concentrations in saline solution. This makes it easy to administer and also makes it necessary to use a fairly large volume of fluid.

The indications for the use of any parenteral sulfonamide drug are the same as those for the drug itself, except that the patient finds it difficult or impossible to take it by mouth, particularly if he is vomiting a good deal, or in extremely ill patients where a few hours are important. In general, it is advisable to stop the parenteral use of the drug as soon as it is possible to give it by mouth. With the high concentrations that are attained soon after injection, the drug is brought rapidly to the kidney, where renal complications are much more likely to occur in the continuous parenteral therapy than when oral therapy is used.

The dosage of drug used parenterally is essentially the same as that given orally. The initial dose is identical. If sulfathiazole is used, it is preferable to divide the subsequent daily dose, if it is necessary to continue it parenterally, into three equal parts, and to give them every eight hours. If sulfadiazine is used, it is possible to give half the daily dose at twelve-hour intervals.

Concerning the use of alkalies, the incidence of untoward renal and urinary-tract complications is somewhat less if the urine is maintained on the alkaline side. It is possible to maintain higher concentrations of the drug in the urine without precipitation in an alkaline urine, as compared with an acid urine, and if renal complications occur, — hematuria and so forth, — the administration of alkalies such as sodium bicarbonate by mouth or sodium lactate intravenously, is advisable. These alkalies are given to the point where an alkaline urine is obtained and maintained. Whether they should be used routinely is a question that depends a good deal on whether one may or may not give alkalies in large amount to the patient whom one is treating. They are not necessary in most cases with the usual dosage of sulfadiazine, provided the fluid intake and output are adequate.

DR. KEEFER: I gather, then, that in giving the sulfonamides parenterally, the sodium salt in 5 per cent solution in distilled water, given intravenously, is *not* the method of choice. If it is dissolved in physiologic saline solution, 0.5 to as high as 3 per cent may be given.

The next question goes to Dr. Janeway: "What is the difference between the use of sulfonamides in children and in adults?"

DR. JANEWAY: I do not think that the fundamental principles are the least bit different. The differences lie in the way children and adults react to disease. Children vomit more readily than adults do. Therefore, one has to resort to parenteral therapy more frequently with them than with adults. Children unfortunately void more or less at will, and not in response to the dictates of convention; therefore it is difficult to keep track of the fluid output. Anyone treating a child intensively has to be more alert in looking for renal complications. With an adult, all one has to do is to have the nurse collect the urine in twelve-hour lots. This can be done in the home by using a quart milk bottle, and it is easy to see whether the output rises or falls. But with children it is not so simple. One has to depend more on the answers of the mother or the nurse, and more particularly on the examination of the urine, looking for red cells. The third thing, which I pointed out before, is that the white-cell count is a fickle guide whether or not one should use intensive treatment in children, because there are so many abnormal responses of children's blood to infections. However, I believe that, taken all in all, the differences between chemotherapy in children and in adults are not great.

DR. KEEFER: Here are two questions for Dr. Davies: "What are the indications for the use of nose drops? What type of base should be used, oil or water?"

DR. DAVIES: The latter question is easy to answer — water. But the indications for the use of nose drops are not quite so simple. I am quite sure that we use them too much. One might say that with a simple rhinitis nose drops are scarcely necessary. However, if the infant is having trouble in breathing at feeding time, some use of shrinking nose drops before feeding is worth while. If there is definite nasal obstruction, especially if there is a purulent discharge, and evidence of sinusitis and otitis, nose drops should be used.

It is hard to choose the types of nose drops, nowadays, because there are so many. We start with ephedrine, 1

per cent in saline solution, sometimes increasing it to 3 per cent. There are various proprietary preparations on the market, some of which now incorporate sulfathiazole or sulfadiazine. But I shall pass the question of the addition of sulfonamides to nose drops over to Dr. Janeway. Personally, I believe that the sulfonamides are not necessary in nose drops, but I am open minded about it; possibly Dr. Janeway will have more definite opinions on the subject.

DR. JANEWAY: I am not open minded about it. I do not think that sulfonamides ever should be used that way. Drugs are coming in that may be effective in these solutions, such as penicillin. I can see no reason for putting the sulfonamides in nose drops, for the simple reason that they do not remain long enough to do any good.

When one is not open minded, one is apt to be wrong. However, I believe that the indiscriminate use of these drugs in nose drops is wrong. It is easy to sensitize people through the nasal mucosa and the skin, and the use of sulfathiazole in nose drops is just as bad as some other uses, such as in ointments for skin infections. The latter should not be used as a routine. In the first place, one can clear up impetigo with agents that are more definitely bactericidal than sulfathiazole ointment, which has to be put on every three hours to do any good. I have seen a number of cases in which sensitivity to the sulfonamides originated from the local use of relatively small amounts of the drug; the patients reacted when given the drug by mouth for more serious infections later on. That is particularly true of sulfathiazole, which is an excellent sensitizing agent, so far as we can find out. The incidence of sensitivity is high.

Since sulfathiazole will be used more in the coming year or two, it is rather important not to employ it in cases in which its value is questionable.

DR. KEEFER: Dr. Finland, will you say something about the problem of sensitization?

DR. FINLAND: This is a rather difficult subject. Certainly some men who are concentrating their efforts on the treatment of allergic children look with awe on those who hand out sulfonamides on the least provocation and even on those who use sulfonamides for all infections. They are afraid that these patients will die some day from a subsequent dose of a sulfonamide drug. At least, so it was said at a meeting of the Academy of Pediatrics.

There is no doubt that sensitization to sulfonamide drugs has occurred. As Dr. Janeway has mentioned, the worst offender is sulfathiazole. Such sensitization can occur at any time, particularly in a patient who has had drug fever or a skin rash or in the rare cases of jaundice. It may occur after the first dose, and may give a very vigorous reaction, with a high fever and chills. I know of a patient who had a high fever with jaundice, and almost a fatal reaction after a single dose of sulfathiazole given a few days after a similar toxic reaction that followed a course of sulfathiazole therapy.

How often sensitization occurs, how long it persists and whether it decreases with time or stays the same are questions that are difficult to answer at present, because the data available are extremely inadequate.

One thing is certain: in general, sensitization to any one drug, in the sense I have mentioned, does not mean necessarily sensitization to all other sulfonamides, and usually it is possible to administer a different drug at another time. If necessary because of the nature of the infection, it is even possible immediately after the discontinuance of one sulfonamide drug to start giving another. Exceptions to this are probably extremely rare.

Sensitization is usually manifested by the occurrence of a fever or a rash, or both, but is sometimes manifested by other phenomena, such as the appearance of jaundice and enlargement of the liver, and in some cases by other reactions, such as those involving the central nervous system, which I have been fortunate enough not to encounter.

DR. KEEFER: General practitioners and pediatricians are using the sulfonamide drugs for almost every infection. They maintain that many children are being saved from otitis and its resultant mastoiditis, bronchitis, pneumonia and, when sulfadiazine is used, possibly meningitis. Some pediatricians are practical minded enough to give these drugs in proportion to the symptoms, and not in proportion to the body weight. Under these circumstances, illnesses are cut short, so that the drugs are used for only two or three days. Dr. Janeway, will you give one and, if possible, two sane reasons why this practice should not be followed in all early cases of respiratory disease?

DR. JANEWAY: This is a difficult question to answer. Many are saying that they give sulfonamides according to the extent of the respiratory infection, and they claim that the illness is short lived and does not lead to complications.

The only thing one can say is that the vast majority of respiratory infections are relatively mild diseases that subside without doing the patient any great harm, and it is questionable whether one should simply administer drugs on a perfectly blanket routine for any sort of infection. One might as well say that any time a person's heart goes faster than 100, one would give digitalis, and I think the reasoning would be much the same.

It is true that the majority of complications of the virus infections that cause the usual epidemic respiratory infections are bacterial in nature, and it is quite likely that a certain number of these can be prevented and diminished in severity by the administration of the drugs. However, against routine is the problem of sensitization, and the extent of that problem we do not fully know as yet. Also toxic reactions do occur. I have no doubt but that in a number of cases respiratory infections may last somewhat longer if chemotherapy is not given. But I prefer, in general, to use the sulfonamides for the treatment of infections rather than for their prevention. The administration of the sulfonamides does not do anything to the cold itself, provided it is a virus cold. In a certain number of colds due to bacterial agents it may be effective.

Concerning why the sulfonamides should be given according to the body weight rather than in proportion to the symptoms, the only answer is that we know definitely from a great body of laboratory evidence that one has to achieve a certain concentration of the sulfonamides in order to control bacterial infection. There is no doubt that a severe infection requires more sulfonamide for its control than does a very mild one. This is because in the mild infection the patient himself is controlling it to a very large extent, and all one does is add a slight deterrent to the bacteria, which enables the patient to overcome the infection. A severe infection is almost always due to a breakdown in the patient's resistance,

and the sulfonamides become the only agents that are really capable of controlling the infection until the patient rallies enough to get hold of it himself. So, to that extent, there is a rationale there.

On the other hand, one cannot cut down the dosage more than to a certain point and expect to get any results, unless one is using the drugs prophylactically. The only studies on this subject are those in the prevention of rheumatic fever. There, it becomes clear that relatively small doses, equivalent to 1 to 2 gm. (15 to 30 gr.) of sulfanilamide or sulfadiazine per day, are effective in the prevention of acute hemolytic streptococcus infection, and because of that, they are effective in preventing occurrences of rheumatic fever.

On the same reasoning, one might say, "Give every patient with a cold these small doses of the sulfonamides." But my own belief is that one does not have to give the drug. Three quarters or more of the colds are taken care of in the usual course of events.

DR. KEEFER: I agree entirely with Dr. Janeway. I do not believe that the sulfonamides should be given to every patient with a respiratory infection. I do believe that they should be given in accordance with the body weight rather than in accordance with the symptoms.

THE LATERAL VIEW IN THE ROENTGENOLOGIC DIAGNOSIS OF LESIONS OF THE COLON*

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BOSTON

IT IS a well-known fact that roentgenologic diagnosis of diseases of the colon, especially those of the sigmoid and rectum, is one of the more difficult branches of roentgenology. The lower colon has repeatedly been called the "dark spot" of the gastrointestinal tract, and this statement has been especially true for the sigmoid and the lower descending colon, the rectum being easily accessible by other means of examination such as the proctoscope and, last but not least, the surgeon's examining finger.

It is, however, surprising as well as depressing to note how many lesions in these areas have been overlooked in the past, and how many are still missed in spite of numerous efforts to approach these regions in a more thorough and methodical manner. These efforts are highly important, since lesions of the lower colon are in the majority of cases malignant or premalignant.

Failure of the roentgenologist to detect early lesions has given rise to a pessimistic attitude on the part of the surgeon that is reflected only too well in the surgical literature. There we find comments such as the following, made by Bowman[1] as late as 1938: "A negative barium enema should not be regarded as diagnostic, since a majority of the tumors of the rectum do not show a filling defect." As a matter of fact, the majority of these lesions do show a filling defect, and the question here apparently is, What are the reasons for the failure of the roentgenologist to demonstrate these defects?

The answer appears to be twofold: the peculiar anatomic conditions of the structures of the lower gastrointestinal tract, and the failure to employ some or all of the helpful procedures that have been devised for the examination of these areas. Let us consider these two points.

Figure 1 reveals why a small tumor situated on the posterior wall of the colon (B) is so easily

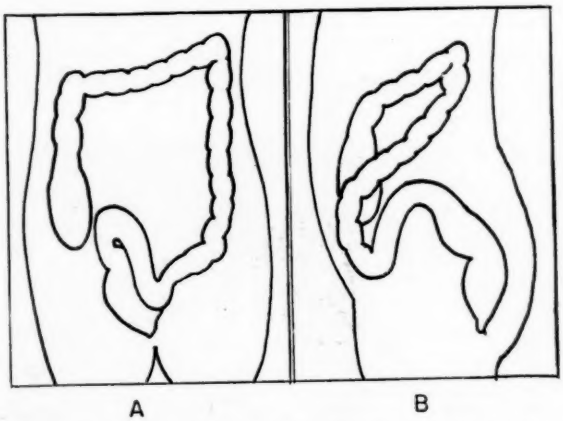

FIGURE 1. *Schematic Drawing Showing the Usual Relations of the Pelvic Segments of the Colon.*

A shows how a tumor in the upper rectal ampulla or in the sigmoid can be completely hidden in a posteroanterior view by overlying unaffected structures. In B, *a lateral view, the rectum and sigmoid are shown in their entirety, with no overlapping of the loops.*

overlooked in the anteroposterior view (A). The tumor is entirely hidden behind the barium shadow of either the completely filled loop of colon or, worse, of two overlapping loops or, still worse, of both. Since the rectum is a wide, hollow tube with the sigmoid arising from it at an oblique angle, there is overlapping of loops of colon in a majority of cases. Knowledge of these anatomic difficulties has led to the development of several

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helpful procedures for the examination of the lower colon and, as a matter of fact, of the entire gastrointestinal tract. It is the purpose of this paper to remind the roentgenologist as well as the surgeon of these procedures, for which no priority is claimed but which unfortunately are not so widely or so routinely in use as they should be.

One of these methods is the double-contrast enema. As early as 1910, Cole and Einhorn[2] advocated the use of air in the examination of the digestive tract, and in 1923, Fischer[3] published his method of double-contrast enemas, which is still in common use, or at least should be. Further studies include the oblique and the lateral view, both routinely used in our x-ray department. The latter has proved particularly helpful in a large number of cases. All these procedures have been published and their importance emphasized, notably

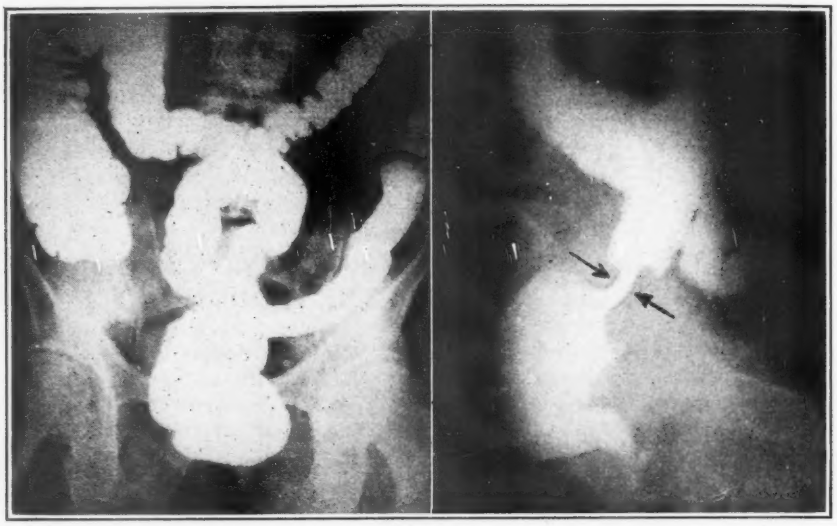

FIGURE 2. *Annular Filling Defect of the Sigmoid (Case 1—adenocarcinoma).*
Note that the defect is well shown in the lateral view but is invisible in the posteroanterior projection.

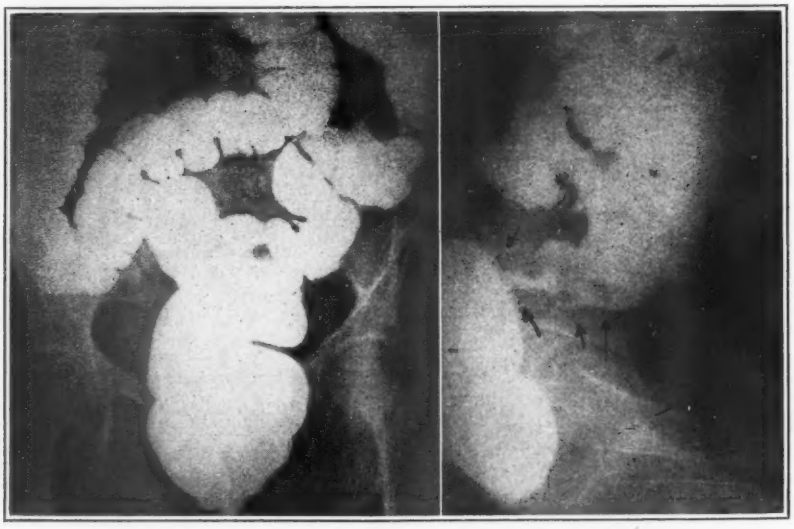

FIGURE 3. *Large Filling Defect of the Sigmoid (Case 2—inoperable adenocarcinoma).*
Note that the defect is not visible in the posteroanterior view but well outlined in the lateral projection.

in the more recent papers by Wolf,[4] Stewart and Illick[5] and Robins and Altman.[6]

We shall present the routine x-ray technic successfully employed in our department, typical case histories and accompanying illustrations.

A word should be said concerning the preparation of the patient. This is as essential a part of the examination as are radiography and fluoroscopy. Without proper preparation, which essentially means cleansing, no adequate examination of the gastrointestinal tract is possible. For the colon, we use the following procedure: On the day prior to examination, 60 cc. of castor oil is given. One should insist on this medication unless a definite clinical contraindication exists. On the evening prior to examination, a high cleansing enema is given. The enema is repeated on the morning of the day of examination. The patient is then brought to the fluoroscopy room and put on the fluoroscopy table in the supine position. The enema is allowed to flow slowly into the rectum, and the patient is repeatedly rotated to the right- and left-oblique positions while being fluoroscoped. Of special value is the right anterior oblique position, which yields a better visualization of the rectosigmoid junction. A spot-film device allows one to take quickly small films of any suspicious area in the position best suited for its demonstration as determined by fluoroscopic examination. The entire colon is then filled to the cecum in the same manner, and a posteroanterior and a straight lateral film are taken immediately on the Bucky table.

After the enema is expelled, the patient is again fluoroscoped. If evacuation has been thorough, the remaining barium coats the colonic mucosa. If too much barium remains, fluoroscopy is repeated after further expulsion. A posteroanterior and a lateral film are then taken. In a majority of cases, it is possible in this way to gain a valuable impression of the condition of the mucosa of the colon. If doubt concerning the diagnosis still remains, a double-contrast enema is employed. The colon is slightly inflated by air and films or spot films are taken. It should again be emphasized that all these examinations are done, and without exception should be done, under fluoroscopic control.

FIGURE 4. *Filling Defect of the Proximal Transverse Colon (Case 3 — carcinoma).*

Note the improved visualization in the lateral view, in which the extent and character of the lesion are clearly shown.

Whereas this procedure is not only time consuming but a little more expensive than others, at least four 14-by-17-inch films being taken, its value cannot be overemphasized.

The following 3 cases and accompanying radiographs are typical of the large number we have examined.

CASE REPORTS

CASE 1. The patient, a 60-year-old man, had had loose stools all his life, recently with some gas and slight weakness but without weight loss. He had never had bloody or tarry stools. On physical examination, he appeared to be fairly well nourished. The head, heart and lungs were negative. The abdomen was slightly tender but no masses could be palpated. On rectal examination, nothing was found with the exception of a slightly enlarged prostate. A barium enema showed a constant annular filling defect in the sigmoid 18 cm. above the anal opening (Fig. 2). A colostomy was done,

and was later followed by a combined abdominoperineal proctectomy, with resection of the sigmoid. The pathological report was adenocarcinoma, Grade 2-3.

Case 2. The patient, a 59-year-old woman, complained of increasing diarrhea,—instead of former mild constipation,—with no abdominal pain but with occasional small flecks of blood in the stools. She had been operated on for a pelvic abscess 1 year previously and had since lost 6 pounds. On physical examination, the head, chest and abdomen were essentially negative and no masses could be palpated. A barium enema revealed an organic filling defect of the sigmoid (Fig. 3), which proved to be an inoperable adenocarcinoma with extensive local and distant metastases.

Case 3. The patient, a 45-year-old woman, had been well until 1½ years previously, at which time she had her first attack of diarrhea. These attacks had since occurred more frequently. She had nausea, indigestion, gas, a weight loss of 35 pounds and pain in the right upper quadrant of the abdomen, radiating to the back. On physical examination, the head and chest were essentially negative. An irregular abdominal mass could be palpated in the right upper quadrant. Roentgenologic examination showed a large organic filling defect in the proximal transverse colon (Fig. 4), which at operation proved to be a carcinoma. No liver metastases or adhesions were found. A transverse ileocolostomy was done.

Cases 1 and 2 are typical of many in our series. The extent and type of lesion are well shown in the lateral view in both cases. They could not have been diagnosed or even suspected from the routine posteroanterior view, for the sigmoid in the affected area ran in a sagittal plane.

Case 3 differed from Cases 1 and 2 in two respects: the lesion was in the transverse colon, and it was visible also in the anteroposterior projection. However, comparison between the two views reveals the markedly increased diagnostic possibilities of the lateral projection. The exact extent of the tumor, the area of annular constriction and the shelving at the borders of the tumor are clearly demonstrated. The posteroanterior view, on the other hand, shows only indefinite disease.

Summary

The advantages of the lateral view in the examination of the colon, with special reference to the sigmoid, are described, and an outline of the technic is given.

Three typical cases are described and illustrated.

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MEDICAL PROGRESS

ORTHOPEDIC SURGERY (Concluded)

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Clostridia Producing Gas Gangrene

CLOSTRIDIA (spore-forming anaerobic gram-positive bacilli) are normally saprophytic. A number of them under suitable conditions may become pathogenic and produce gas gangrene, and one of them is the cause of tetanus, which is discussed in the following section.

Gas gangrene is a mixed infection, but certain of the clostridia are usually essential etiologic factors. Anaerobic putrefactive nonhemolytic streptococci may, however, produce an infection at present indistinguishable from gas gangrene.

Clostridium welchii (Bacillus perfringens), Cl. septicum (B. oedematis maligni or *Vibrion septique), Cl. oedematiens* (Novy) and *Cl. oedematoides* (Sordelli) are each capable of producing serious gas infection. One usually predominates in association with one of the others and also with one or several of the following less important clostridial pathogens that may augment the infection: *Cl. histolyticum, Cl. fallax, Cl. sporogenes, Cl. lentoputrescens (putrificum) and Cl. bifermentans.* These latter, while contributory to the infection, do not alone seemingly possess sufficient aggressiveness to cause clinical gas gangrene and toxemia. These clostridia may be found in gas infection in association with many other bacterial species, both aerobic and anaerobic, including hemolytic streptococci.

Identification. Because fatal gas-bacillus infection may become established with great rapidity, early etiologic identification is of the utmost importance. This cannot await cultural studies but must depend on local signs, although toxic manifestations may be strikingly significant. The mere presence of considerable numbers of large gram-positive bacilli in smears of wound exudate does not establish a causal relation. Local signs include the following: gas, evidenced by fine crepitus on gentle palpation about the wound, by bubbles expressed from the wound through the exudate, or by x-ray study; odor — putrefactive and mouse-like smells, the latter being seldom present but when found being diagnostic of infective gangrene of muscle (Qvist[21]) and at once stamping the infection as serious; and local pain and edema, which may be conspicuous. *Cl. oedematiens* when predominant may produce a lesion characterized by rapidly progressive massive edema with little or no gas or odor but with profound toxemia. In gas infection, toxic manifestations vary with virulence and toxigenicity and are therefore not dependable under all circumstances. There is an abrupt rise in pulse — the first sign of onset. This is especially noteworthy if accompanied by a rise of blood pressure. The temperature may be high (up to 105°F.) in patients with good resistance, but slightly elevated in mild infections; if subnormal, with rapid, thin pulse and other signs of shock or hemorrhage, it is a bad prognostic sign.

Identification by cultural methods should be made immediately for subsequent specific antitoxic therapy, but this should not delay operative intervention or the immediate administration of polyvalent antitoxic serums.

Toxic factors. A number of toxins can be demonstrated, and considerable study has been made of their action in animals. Toxic effects in man, although they may be profound, have not been clearly defined (Wright[7]). Each of the group produces a specific antitoxin.

Source. Pathogenic clostridia are normal inhabitants of the intestinal tract of man and domesticated animals. They persist for long periods as spores in soil, especially where manure has been used as fertilizer, and in street dirt. However, analyses of the flora of fresh wounds, inflicted under widely diverse circumstances, commonly reveal the presence of clostridia capable of producing gas infection, often in considerable numbers. There is therefore ample justification for assuming the presence of pathogenic clostridia in such wounds regardless of the circumstances attending their infliction.

Pattern of infection. Gas bacilli are normally anaerobic saprophytes. They do not become pathogenic unless certain conditions peculiar to their needs exist in the wound. The condition fundamental for pathogenicity is a sufficiently low concentration of oxygen in the involved tissues to allow the spores to germinate, the bacilli to multiply, and toxins to be produced. This con-

The articles in the medical-progress series of 1941 have been published in book form (*Medical Progress Annual.* Volume III. 678 pp. Springfield, Illinois: Charles C Thomas Company, 1942. $5.00).

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dition is apparently created as a result of impairment of the blood supply to the part either by local trauma, by vascular shock or injury or by vascular degenerative changes or by a combination of these.

Clostridial gas infections vary widely from innocuous and self-limiting to fulminating and hopeless. Other factors being equal, the severity of the infection is dependent on the tissue involved: those infections that are confined to cellular connective tissues are mild, and those established in devitalized muscle are apt to be grave and give gas gangrene its evil name. This distinction, recently re-emphasized by Qvist,[21] must be clearly recognized. It is of great importance, both clinically and academically. Clinical differentiation between the two types of infection is definite.

In the first place, infections of cellular connective tissue by clostridia are probably much commoner than those in devitalized muscle. The inflammatory reaction is a cellulitis in general comparable with that of other organisms and noteworthy in respect to gas formation and gangrene. The infection may remain localized in the devitalized elements and cease when these have been exhausted; or it may spread slowly along fascial planes and subcutaneous tissues. So long as muscle is not involved as a rule the infection remains relatively mild: the mousy smell of muscle involvement is absent, and toxemic manifestations are not severe — the temperature is commonly not high, although the pulse rate is often considerably elevated. Although these signs are indistinguishable from those of early muscle infection, they are not comparable with the profound toxemia of a well-established infectious gangrene of muscle. This mild form of infection, often self-limiting and commoner in civilian than in military practice, may well explain the cures claimed for x-ray therapy in gas infections.

In the second place, when muscle is infected by gas bacilli, sepsis spreads rapidly and toxemia is profound. Under favoring conditions clostridial saprophytes present in the wound develop a striking virulence, which is quickly enhanced — within a few hours — by toxigenicity and invasiveness. Bacteria swarm through the injured portion of the muscle, destroying it. Next, the muscle distal to the wound, having a diminished blood supply but being still somewhat viable, is invaded. Extension occurs along the interspaces between fibers, which become choked with exudate and bacteria. The exudate is free of leukocytes unless the infection is complicated by pyogenic cocci. Disintegration of sarcolemma ensues, and the muscle fibers are then entered and disintegrated by the bacteria. Fascial planes afford favorite avenues of extension. Invasion is considerably facilitated by thrombosis, which cuts off the blood supply, thus offering a new field for bacterial spread. Metastatic infection to distant muscle groups is sometimes seen. It occurs through septic embolism, but as a rule the clostridia cannot survive in the blood stream. Invasion proximal to the wound is not held in check for long. Uninjured muscle with an intact blood supply may provide a barrier for only a short time, often not long enough for the surgeon to intervene before it is too late. The infection may involve a single muscle — more commonly a muscle group — or a segment of a limb. The skin at the wound margin passes slowly and progressively through phases of redness, bronzing, duskiness and finally the blue and black of necrosis. The extent of skin gangrene is always far short of that of muscle necrosis. Gas formation may be apparent late or not at all. It is usually present to some degree, being revealed by gentle palpation as a fine crepitus, by x-ray examination or by bubbles expressable from the wound through the exudate. Gas formation may be profuse, at which time the margin of the crepitant area may show appreciable advance at 30-minute intervals and extend far beyond the infected region into healthy tissue. A mousy odor, often present, is diagnostic of gas infection of muscle. Rapidly spreading edema, more or less marked, is almost always one of the characteristics of the local sepsis. Clinical toxic manifestations include malaise, restlessness, apprehension and, later, prostration. An abrupt acceleration of pulse (to 120 or 130), accompanied by a rise in blood pressure, is very significant. The temperature may reach 105°F., but in patients with low resistance and a poor prognosis may be subnormal.

Cl. welchii and *Cl. septicum* are conspicuous producers of gas, and *Cl. oedematiens* of massive gelatinous edema. All these clostridia are profoundly toxigenic.

Uncommonly the muscle type of infection may be fulminating, with little or no demonstrable local edema, gas, odor or pain but with profound toxemia, accompanied by a cold pale dry skin, a pulse too rapid to count and a subnormal temperature. *Cl. welchii* has been shown to be responsible for this symptom complex; however, the same state may be produced by an anaerobic nonhemolytic streptococcus.

Management. Prevention of infection by a complete débridement, as discussed below, within four to six hours of wound infliction, supplemented by prophylactic serotherapy and chemotherapy,

largely solves the gas-bacillus problem. Animal experimentation supports the use of the sulfonamides in cases in which infection with *Cl. welchii* or *Cl. septique* — but not with *Cl. oedematiens* — is a possibility. Sulfanilamide is the drug of choice at present, 6 gm. being given orally as the initial dose, followed by 1 gm. every four hours for seven days; locally the crystalline form is sprinkled evenly over the wound surfaces, 0.1 gm. per square inch — but not over 10 gm. in all. The prophylactic use of polyvalent antitoxin in injured persons not sensitive to the serum is also indicated as a supplement to early débridement. The dose should be adequate and is specified on the container of the preparations in use.

The early recognition of established gas infection may be of vital therapeutic importance. To this end, patients with wounds involving muscle damage should be frequently checked — every two or four hours — for mousy odor and abrupt rise of pulse. Time is essential in many of these infections. When the diagnosis has been made, the appropriate surgical procedure is carried out without delay. Chemotherapy is begun at once, if it has not already been instituted, and in this regard much time may be saved by intravenous administration. Sulfathiazole is the present drug of choice. Polyvalent antitoxin is administered in large and frequent doses, both intravenously and in the muscle — by some being injected into the normal muscle about the wound. An initial dosage of four to six standard therapeutic doses is followed by two to four standard doses every four to eight hours until the infection is under control. When the responsible organisms have been identified in the laboratory, the corresponding specific antitoxins are used in place of the polyvalent.

The surgical procedure to be adopted depends on the type of tissue infected and on the nature and extent of the infection. Infective gangrene of muscle demands either radical extirpation of devitalized or necrotic tissue and the removal of foreign bodies, or amputation. Infections involving only the cellular connective tissues and not the muscle may be sufficiently dealt with by removal of sutures and a wide opening of the wound — possibly with simple incisions in addition. The mere presence of gas in a wound and numerous large gram-positive bacilli in a stained smear of the exudate does not justify amputation. The sacrifice of a limb superficially infected as in gas cellulitis is unnecessary and reprehensible. On the other hand, to withhold radical extirpation of an infected muscle or group of muscles in the belief that the infection is confined to the cellular tissues, is to court disaster. In extensive, rapidly spreading muscle gangrene involving whole segments of a limb, amputation, if possible at a remote level, must be done promptly as a life-saving measure. Table 1 differentiates these two types of infection and their treatment.

All gas-infection wounds, whether the treatment has been simple incision, débridement or amputation, are left wide open. Meleney[22–24] advocates a loose packing, saturated with a creamy suspension of zinc peroxide — which must be of fresh medicinal grade — in sterile distilled water. The suspension is made just prior to use by adding the peroxide powder, sterilized in a dry sterilizer at 140°C. for four hours, to an equal volume of sterile distilled water. The wound is flooded with this suspension before the packing is placed, care being taken to reach all parts of it. The packing is covered with a thick layer of absorbent cotton soaked with distilled water, and the whole is covered with vaseline gauze to check evaporation. This dressing is changed daily. Trueta[25] advocates a loose sulfanilamide pack.

Immobilization of the limb is essential, and fluid balance (2000 to 4000 cc.) must be maintained.

TABLE 1. *Signs and Symptoms, and Treatment, of Cellulitis and of Gangrene of Muscle.*

CELLULITIS	GANGRENE OF MUSCLE
Signs and symptoms	
Relatively mild localized sepsis and mild toxemia	At first relatively mild and localized; quickly becomes violent, spreading sepsis and profound toxemia.
Odor putrefactive, but mousy smell lacking	Mousy odor
No involvement of muscle at operation	Definite change in appearance of muscle, which may be hemorrhagic or discolored, may not contract normally on pinching, or may bleed abnormally slowly or not at all
Treatment	
Open wound widely, with incisions if necessary	Radical débridement; amputation (guillotine or, if favorable, open-flap method).
Pack loosely and open with sulfanilamide pack or zinc peroxide dressing	Same as for cellulitis

Clostridium Tetani

Cl. tetani, a strictly anaerobic gram-positive bacillus with a terminal rounded spore, is at present recognized in nine different serologic types. These vary in their agglutination reactions, but all produce lethal exotoxins that are identical antigenically.

Toxic factors. The clinical manifestations of tetanus are due to the toxin produced by *Cl. tetani*. The disease in its typical form can be produced by the injection of the toxin alone. Two components can be demonstrated, a hemolysin (tetanolysin) and a toxin selective for nervous

tissue, especially motor cells (tetanospasmin). Local sepsis by the organism may be negligible or not even appreciable; it is noninvasive. Although a strong affinity exists between the toxin and nerve tissue, recovery is attended by no apparent nerve impairment. There probably also exists an affinity between the toxin and muscular tissue or the myoneural junctions. Antitoxin completely neutralizes free toxin, but has no effect on that already fixed by the nervous system.

Source. Cl. tetani is a common inhabitant of the intestinal tract of horses, cattle, sheep and fowls, and is found in soil, being especially abundant in that fertilized by manure. Human (intestinal) carriers constitute a fair proportion of the community. Spores may survive for many years in the tissues. Wound infection is prone to occur in those engaged in agricultural pursuits and in soldiers, although no group of persons entirely escapes the disease.

Pattern of infection. Cl. tetani is commonly saprophytic, and it is virtually impossible to infect healthy tissue with the spores. Under certain conditions, however, the organism becomes fatally pathogenic, solely by virtue of its toxin. Wound factors necessary to pathogenicity include the following: devitalized tissue, foreign bodies, especially dirt or the coexistence of infection by other organisms, and a reduced oxygen tension locally. Any wound in which any or all of these conditions exist is a potential source of tetanus. Although occurring by far the most frequently in war wounds and in those of people who work in the soil or about domesticated animals, the infection may appear in any wound, including burns, bites, powder (Fourth of July) burns, bedsores and operative wounds — more especially in the intestines and about the anus. It may be caused by nonsterile catgut used as suture material. Experience in World War I demonstrated that a wound may heal fully without the appearance of tetanus, only to develop tetanic infection following subsequent operation. In such cases the spores remain inactive because the conditions necessary for germination and growth were originally lacking, and also by reason of the prophylactic use of antitoxin. The eventual loss of the passive immunity conveyed by the latter, together with the creation of conditions favoring infection by a second operation, permits the development of the infection. For this reason reconstructive operations on wounds that may harbor the spores of this organism must be preceded by another prophylactic injection of antitoxin.

The incubation period of tetanus is usually seven to fourteen days, but the disease may appear as early as one day or after two hundred days. Under favorable conditions the organisms multiply slowly but do not become invasive and do not appear to produce an appreciable septic reaction when the infection is unmixed. They have been recovered from regional lymph nodes, but not from the blood stream. Metastatic infections do not occur. There is much evidence to substantiate the view that the toxin is absorbed by the lymphatics, through which it reaches the blood stream, and by the latter is conveyed to the central nervous system. The former belief that toxin reaches the brain and cord by way of the peripheral motor nerves is no longer regarded as tenable (Abel et al.[26–30] and Firor et al.[31, 32]).

Clinically the disease is found in two forms: local or ascending, and general or descending. In the local form, rigidity, sometimes contractions and less often spasm occur in muscles of the region of the portal of entry. These may be mild and disappear spontaneously, or may increase in intensity and extent, becoming the generalized form. In general tetanus the rigidity begins in the facial muscles and spreads slowly downward to include the musculature of the neck, trunk and extremities. Muscular rigidity progresses to spasm and then to clonic and tonic contractions, which may extend from localized groups into violent generalized convulsions. Trivial stimuli may initiate these seizures, which may become continuous, and finally death supervenes from asphyxia or exhaustion. It should be clearly recognized that at the time of the first sign of tetanus (muscular rigidity) the disease has already become established.

Management. Active immunization by toxoid to prevent tetanus bids fair to score a high mark in the present war. What few cases appear to develop following its use have a relatively low mortality. Such immunization, combined with prompt and skillful débridement of wounds and the administration of antitoxin, removes the serious menace of the disease.

Active immunization by toxoid consists in three subcutaneous injections of 1 cc. of the alum precipitate of the toxin at three-week intervals. This initial vaccination is supplemented by a stimulating dose of 1 cc. of the toxoid to those who incur wounds that might harbor the clostridium and also to those who are about to undergo secondary open or manipulative procedures and who have not within three months received toxoid.

In cases in which the patient has not received the initial vaccination and presents himself with a potentially dangerous wound, a dose of 1500 to 3000 units of antitetanus serum is injected subcutaneously to confer passive immunity. Prior to injection with serum the following sensitivity tests are carried out: Inject intracutaneously 0.1 cc. of a 1:10 solution of serum in sterile physiologic saline solution. The patient is sensitive if, after

twenty minutes, the wheal has enlarged to the size of a nickel and is surrounded by a reddened area. Next, instill in the lower conjunctival sac 1 drop of a 1:10 dilution of serum in sterile physiologic saline solution. The test is positive if, within twenty minutes, the eye is reddened and swollen. In addition to injection for passive immunity, the patient should be given the regular course of initial vaccination.

The problem of the management of established tetanus is one of protection of the patient against all stimuli possible, control of spasm by deep sedation, stopping the production of toxin by the wound, ridding the blood stream of free toxin, maintenance of general strength by adequate caloric intake and fluid balance and measures to prevent suffocation. To these ends the following measures have the stamp of approval of those[33] who have given this disease the most study. The patient is secluded in a quiet, darkened room. Sedation is worked out according to the patient's best individual response. It may consist in the administration of paraldehyde by rectum, 8 to 40 cc., repeated every four hours, of chloral hydrate by rectum or orally, 1 to 3 gm., repeated every four hours, or of Avertin by rectum, 0.03 to 0.06 gm. (½ to 1 gr.) per kilogram of body weight. If cessation of breathing is impending, artificial respiration is mandatory; for this the Drinker respirator is best. Asphyxia from laryngeal spasm demands tracheotomy. The administration of antitoxin is delayed only long enough to test the patient for serum sensitivity (if the test is positive, desensitization is obligatory). One hundred thousand units of the antitoxin is given on the first day, as follows: 5000 to 10,000 units by infiltration about the wound, 60,000 units intravenously, and 30,000 units intramuscularly. On each of the subsequent days 5000 units is given intravenously until the attacks abate. Intravenous administration must be very slow. If the anaphylactic reaction appears, the needle is at once withdrawn and 1-cc. doses of 1:1000 adrenalin are repeatedly injected into the muscle until the symptoms of shock have stopped. About an hour after the infiltration of antitoxin around the wound, excision of the portal of entry is carried out if feasible. If this is not possible, thorough débridement is substituted. A fluid diet of 2000 to 4000 calories, preferably by a nasal tube, and a fluid intake of at least 3000 cc. are necessary to maintain the general condition.

Preferential Anaerobic Streptococci

The bacteriologic status of this group has not been clearly defined. Culturally these organisms exhibit a strong anaerobic tendency but not strictly so; they are found in both hemolytic and nonhemolytic forms. They are highly pathogenic under special conditions, which are somewhat indefinite. Such streptococci may be recovered in pure culture from chronic undermining ulcerations (Meleney[34]) that develop in the subcutaneous tissue, either in a traumatic wound or in one created surgically to drain an infected lymph node or for some procedure upon the intestinal or genitourinary tract. It is believed that the organism is an aerobic streptococcus altered by residence in the intestinal tract or in a lymph node. It may also produce gangrenous infection of the skin in synergistic association with *Staph. aureus.*

Identification. This is by anaerobic culture, but the organisms from some lesions may be grown aerobically.

Pattern of infection. In chronic undermining ulcers, the infection is confined to the cellular connective tissues, fat and fascia, which it liquefies. Spread is slow but persistent, undermining but not infecting the skin over a wide area and burrowing along the deep intermuscular septums. Erosion of large vessels or amyloid changes may cause death after months or even years unless the patient finally gets the upper hand or the organism is eradicated by treatment. Toxic manifestations include prostration, wasting and daily rises in temperature to 103°F.

In bacterial synergistic gangrene of the skin, the lesion is confined to the skin and arises at the margins of operative abdominal and chest wounds created for the drainage of peritoneal, pleural or lung abscess. It develops slowly — during the first week or two following operation — as an edematous, exquisitely tender area of erythema. In a few days the central portion takes on a purplish hue, which slowly spreads as the area of erythema advances and there then develops frank gangrene in the portion where the purplish area first appeared. This results in a skin lesion that is gangrenous centrally and erythematous peripherally, with a purplish intermediate zone. On the central side the purplish band is sharply defined and crenated, whereas on the peripheral side it gradually blends into the reddened zone. The involved area is raised above the surrounding healthy skin. Liquefaction of the gangrenous area takes place centrally as the infection spreads. Anaerobic culture of the tissue in the reddened zone reveals the presence of these preferential anaerobes alone, whereas the tissues in this zone are hyperemic. In the gangrenous zone *Staph. aureus* is found in association with this streptococcus. The purplish zone is edematous and is the seat of dense cellular infiltration. The two organisms are believed to produce the lesion by synergistic action, since neither alone can reproduce the infection experimentally but do so when combined. The source

of the streptococci is believed to be the intestinal tract and the staphylococcus comes from the skin or is an air-borne contaminant (Meleney[36]).

Management. In chronic undermining ulcers, the deeper ramifications and sinus tracts resulting from burrowing are laid open widely so as to make readily accessible every recess throughout the system of infected tissue. Otherwise treatment will not be successful. Meleney's zinc peroxide dressing has usually been successful provided the suspension has access to every part of the wound. Oral sulfonamide therapy is a valuable adjunct. Hurwitz and Prien[35] were able to clear up this infection with locally applied sulfonamide after failing with zinc peroxide. When the infection has been eradicated, skin grafting may be necessary to cover wide, denuded areas. Where burrowing has occurred, vigilance is required to prevent fatal hemorrhage from spontaneous rupture of a major vessel weakened by erosion. Every effort should be made to maintain optimal nutrition.

In synergistic gangrene of the skin, excision of the entire focus, including a zone of healthy skin, eliminates the infection. Zinc peroxide dressings are applied to prevent recurrence. Skin grafting is necessary later to cover the defect.

Anaerobic Nonhemolytic Streptococci

Morphologically, the anaerobic nonhemolytic streptococci are similar to other streptococci; culturally they are strictly anaerobic and produce gas and a putrid odor, but not hemolysis. There seem to exist a large number of strains. Adequate classification does not exist, from which it may be inferred that our knowledge of these organisms is less complete than that of the aerobic groups.

Source. These organisms are normal inhabitants of the mouth and upper respiratory, gastrointestinal and female genitourinary tracts, but may be present on the skin and clothing as contaminants. From any of these sources they may enter wounds by inoculation.

Pattern of infection. Normally harmless saprophytes, these organisms may uncommonly become highly virulent. The condition at least partly responsible for this change in behavior is the low oxygen tension found in necrotic tissue or in that devitalized by trauma or a diminished blood supply. In some anaerobic streptococcus infections the organism is found in pure culture; in others, symbiosis is believed to be a definite factor in activating them, the other organisms being *Staph. aureus* or gram-negative anaerobic (fusiform) bacilli and spirochetes. The infection is putrefactive; the pattern varies. It may follow the clostridial form to produce a condition indistinguishable from gas gangrene, or the aerobic streptococcus form, with rapidly spreading cellulitis and severe toxemia and, like the latter, possibly followed by intravascular sepsis, septic embolism, infarction, bacteremia, cardiac valvulitis and metastasis, including that of the bone, or a symbiotic form found in cases of human bite and characterized by intense edema, gas formation and putrid discharge. Each of these conditions is grave, or at least serious.

Management. These infections are best dealt with by excision, amputation or débridement, depending on the region involved. The resulting wound should be treated by the zinc peroxide technic. Sulfonamide therapy may be tried. Anaerobic nonhemolytic streptococcus antiserums have not been developed. For a complete résumé and bibliography the reader is referred to Sandusky, Pulaski, Johnson and Meleney.[37]

Bacteroides and Fusiform Bacilli

The bacteroides and fusiform bacilli comprise a large group of pathogenic, gram-negative, anaerobic bacilli that are non-spore-forming. About them relatively little is known. They are frequently found in fresh wounds together with the common pathogens (Pulaski, Meleney and Spaeth[2]). The designations refer to shape, the bacteroides having round ends, and the fusiform bacilli pointed ends. Their role as infectious agents may be confined to an intense local necrotizing action attributed to a powerful endotoxin.

Treatment of Wounds

The seven cardinal principles that constitute the modern treatment of wounds rest on the basis of natural resistance to bacterial infection and the innate capacity of tissue to repair. These are as follows:

A minimal time between the infliction of the wound and the institution of definitive treatment.
The control of shock.
The excision of devitalized and necrotic tissue and the removal of foreign bodies.
Drainage by exteriorization.
Rest by immobilization.
The maintenance of a normal nutritional state.
Immunotherapy and chemotherapy.

Time Factor

Given similar conditions, the aftereffects of a wound are directly proportional to the time interval between infliction and the coming into active play of all the various measures directed to combating the trauma. Prompt first aid, including the control of hemorrhage, emergency splinting, morphine sedation and plasma transfusion,

is effected to combat shock at its inception. The immediate oral administration of a sulfonamide drug assures its effective concentration in the blood stream at a time when it is most needed to check bacterial invasion. By efficient stretcher and ambulance organization (automobile and airplane) the excision of devitalized tissue, removal of foreign bodies and institution of adequate drainage may be carried out within a few hours or less, when these measures are extremely valuable. The early reduction of a fracture and adequate internal and external fixation are thus made possible. Intravenous chemotherapy — if the sulfonamide has not previously been given orally — and the early administration of prophylactic clostridial antitoxin may only by such prompt action avert grave infection. Prior active immunization against tetanus now seems assured.

Shock

If shock develops, in spite of all efforts to prevent it, the condition should be treated by modern accepted methods, which are outside the scope of this paper.

Débridement

Débridement by its present-day definition specifies the early and wide exposure of the entire wound, and the excision of tissue traumatized by the forces inflicting the wound and of hemorrhagic tissue. It also specifies the removal of foreign bodies and blood clot. For full realization of the benefit of this procedure as an antiseptic measure, knowledge, judgment and skill of the highest order are often necessary. Scientific investigation and clinical experience incriminate necrotic, devitalized and hemorrhagic tissue, blood clot and foreign bodies on the ground that they are culture mediums suitable for pathogenic bacteria. Conversely, healthy tissue is highly resistant to infection. In the creation of such bacteria-favoring conditions in tissue two factors predominate: local trauma and ischemia. Ischemia is present as a result of local vascular injury or of a contemporary remote injury to a major vessel supplying the injured region. Another and constant, more or less influential element in the production of ischemia is regional vascular spasm, the result of local shock and mediated by the sympathetic nervous mechanism. This produces local anoxia and edema, which may promote further ischemia by pressure. Vascular spasm has long been recognized as a factor of considerable importance in activating anerobic bacteria — for example, those producing gas gangrene — by the creation of anoxia. Foreign bodies, such as bits of clothing, metal and dirt, are notorious and persistent contaminators that may cause a wound to remain open, draining indefinitely, and the removal of which may result in prompt healing of the wound. The extirpation of these various infectious niduses is the purpose of débridement. Obviously, the earlier this is done the better. Débridement may be classified as a prophylactic antiseptic method.

The skin should be thoroughly washed with neutral soap and water over a wide area around the wound; the region is shaved if at all hairy and the soap-and-water washing is repeated. The area is rubbed with gauze saturated with benzene to remove grease and dirt, and then with gauze saturated with 70 per cent alcohol until clean. Finally it is painted with a 1 per cent iodine and 1 per cent potassium iodide alcoholic solution, care being taken that the solution does not enter the wound (Nye[38]).

The incision should be axial and not transverse, except that in crossing the flexor aspect of a joint of an extremity the axial elements above and below are connected by a transverse element along the joint crease. It should be ample, so as to allow free visual exploration of all wound recesses. It should be placed, if possible, so as to correspond to a standard accredited approach to the depths of the region wounded and at the same time to include the center of the wound.

The jagged and necrotic skin margins of the wound are excised for a distance of 3 to 6 mm. Skin is resistant tissue with a good blood supply and should not be ruthlessly sacrificed. In cases in which avulsion of the skin has occurred, however, Farmer[39] has shown that nothing short of complete excision of the avulsed portion, removal of every vestige of subcutaneous fat and reapplication of this skin as a free full-thickness graft will alone suffice to save it. This has been repeatedly confirmed.

Fat is nonresistant and has a poor blood supply, and when at all devitalized favors bacterial activity. It is a pernicious obstacle to vascularization. When under the slightest suspicion it should be widely excised. The fasciae and septums require close scrutiny for small hematomas and traumatized portions easy to miss. Cleansing with physiologic saline solution will brighten fascia, giving it a fresh appearance, and will disclose fraying, dirt and other small foreign bodies and hematomas that might otherwise be overlooked. Such tissue is especially favorable to hemolytic streptococci and should be widely excised.

Severely traumatized and hemorrhagic muscle cannot survive and is destined to provide a virtually ideal bacterial pabulum. It may be recognized by its discoloration, by loss or impairment of contractility on pinching and (the most reliable test) by diminished bleeding — that is, absent or lessened oozing — on section. All such muscle

must be excised (by scissors) well into the normal tissue.

All but grossly necrotic portions of tendon should be spared. Damaged sheaths must be excised. Divided tendons should be sutured, if possible, using fine tantalum wire.

Both vessels and nerves are resistant to infection if conditions are at all favorable. For this reason and because of their function, they should be carefully preserved. Damaged arteries should be ligated. Severed nerves should be sutured, if possible with fine stainless steel or tantalum wire or else with fine silk.

Considerable nicety of judgment is required in the removal of bone fragments in a compound comminuted fracture. Pieces of small size (5 mm. or less) devoid of periosteum or other source of blood supply should unquestionably be removed as noxious foreign bodies. Larger fragments, undoubtedly dead, may or may not be rightly removed. Such fragments apposed to normal bone and fixed to it absolutely may serve as massive grafts that are quickly replaced by living bone, and play an important favoring role in the bone-healing process. Large defects at the site of fracture are, no doubt, advantageous from the standpoint of avoiding bone infection, but they exact a terrible toll in terms of time, loss of function and nonunion. Furthermore, before removing sizable fragments the surgeon may well recall that a fractured bone is a decompressed one and need not necessarily become badly infected. On the contrary, absolute fixation by plate or screw may be expected to protect the bone from serious infection, because it is motion at the site of fracture and not internal pressure that fosters infection of bone in these cases. One may well bear in mind, too, that osteomyelitis caused by local contamination in compound fractures, at least in civilian practice, does not imply the low resistance to specific infection found in the hematogenous form. Aside from the problem of removal of fragments, bone débridement is characterized by the care exercised to conserve periosteum and blood supply.

In the methodical layer-by-layer débridement of a wound, hemostasis must be almost absolute. Fine clamps are used to minimize tissue crushing, and ligatures of cotton, silk and fine catgut are used in that order of preference. If possible, instruments are changed with each layer.

On the completion of the excision the entire wound is irrigated from within outward with large quantities of sterile saline.

The above description applies to emergency or prophylactic débridement. Therapeutic or delayed débridement is practiced according to the same principles, except that the barrier raised by the local tissue in the inflammatory fixation must not be crossed. It thus becomes a procedure of excision of necrotic tissue that would otherwise have to be sloughed off, the removal of clot and foreign bodies and the exteriorization of undrained recesses.

It is of the first importance to culture excised tissue and exudate aerobically and anaerobically in order that accurate knowledge of the pathogenic flora may be gained from the outset. In this way subsequent management may be effectively conducted.

Drainage

Clean incised wounds, débrided early in robust patients in civilian practice, may be closed without drainage provided close follow-up and complete postoperative immobilization are possible. Such wounds may be expected to heal by first intention in a considerable proportion of cases. On the other hand, freedom from infection in extensive lacerated contused and dirty wounds and in all war wounds is not to be expected. However, early complete healing of such wounds by secondary intention should be provided for by adequate drainage. Transverse incisions of the aponeurosis are therefore made to decompress the wound and anticipate subsequent edema. The entire wound is then packed loosely with gauze saturated with boric acid ointment or vaseline to hold apart gently the walls of the wound. Such packing does not impede the clearance of discharge, irritate the tissue, or in any way promote anaerobic infection. The wound is protected against subsequent contamination by an ample dressing and the region is immobilized by appropriate external fixation.

Immobilization

The broad principle involved in immobilization is the curative effect of rest. A number of factors combine to this end. These may be divided into three groups: the control of pain, the control of absorption and the control of subsequent trauma.

Immobilization of the injured part reduces the painful afferent nerve stimuli arising out of the wound itself. These are caused by motion in the injured region, by muscle spasm and by pressure from edema. General shock is thus markedly lessened and local muscle, and sympathetic vascular spasm can subside and disappear. There results in turn subsidence of edema, with the result that there is further lessening of the pain factor.

Experimental evidence indicates that the absorption of toxic substances resulting from tissue damage, of bacterial toxins and of bacteria themselves takes place largely through the lymphatics, and it has been demonstrated that the rate of lymph flow is greatly reduced by immobilization, not only physiologically but in the presence of

edema and inflammation (Drinker and Yoffey[40] and Barnes and Trueta[41]). It is well known, furthermore, that toxins that are lethal in massive dose may be neutralized and eliminated without demonstrable ill effect if their rate of introduction to the blood stream is relatively slow. Clinical experience has repeatedly demonstrated the minimizing effect caused by immobilization on many toxemias.

Splinting favors wound repair by protecting new tissue capillaries from abnormal tension, twisting and bending, that is, from the repeated subsequent minor traumas caused by motion. These retard healing, lead to dense avascular scar tissue and cause mechanical spread of infection.

Nutrition

The influence of diet on wound healing has been discussed thoroughly in a previous progress report (Holmes[42]). In general, the optimum diet for patients with infected wounds is one of high-calory, high-polyvitamin content, and this is so selected that the protein fraction is raised at the expense of the fat. Whereas the role of vitamin C deficiency in arresting the formation of intercellular substance (collagen and osseomucin) has been clearly defined, that of vitamins A and D in wound healing and in resistance to infection has not. There is in surgical infections an excessive demand for vitamins that quickly depletes the reserve supplies unless these are maintained either by diet or by direct administration. Increased attention is being paid to the part played by blood protein in tissue repair and resistance to infection and in combating the toxemia resulting from infected wounds. All the evidence points to the importance of this factor. Infection with toxemia causes a drop in the production of plasma protein, and conversely hypoproteinemia lowers resistance to infection, retards tissue repair, lowers general body tone and causes edema. The control of the protein reserve balance in the plasma and tissues in cases of wound infection has not yet been effected. Protein ingestion by mouth has so far proved to have the best effect. Repeated whole-blood and plasma transfusions have not been especially effective in raising the protein level of the blood.

Immunotherapy and Chemotherapy

The various applications of immune serums and the use of toxoid have already been discussed under management of the different infections.

The bacteriostatic property of the sulfonamides when given orally or intravenously is so clearly and widely appreciated that no further comment is required here. The local application of these drugs to fresh wounds combined with oral administration is still a somewhat controversial point, and scientific evaluation is still lacking. One may detect a tendency away from their topical use on the clinical ground that most wounds do as well or better without as with these drugs, and on experimental grounds because of their being prone to act as foreign bodies when not dissolved, because of their toxic effect on tissue cells in high concentration, because of their inability to penetrate devitalized or necrotic tissue, and because their bacteriostatic action is inhibited by wound exudate. On the basis of physical properties — greatest solubility in serum, greatest wound diffusion, most rapid clearance from the wound and quickest excretion — sulfanilamide seems best adapted to this use. The crystals should be evenly sprinkled over the surfaces of the wound in an amount not to exceed 0.1 gm. per square inch of wound surface. For a critical review, the reader is referred to Lyons and Burbank.[43]

I am indebted to Dr. Champ Lyons for help in the selection of sources.

266 Beacon Street

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**
BENJAMIN CASTLEMAN, M.D., *Acting Editor*
EDITH E. PARRIS, *Assistant Editor*

CASE 29301

PRESENTATION OF CASE

A fifty-five-year-old widow entered the hospital because of painless jaundice of two weeks' duration.

The patient had been in good health until three months before entry when she began to experience a feeling of pressure in the epigastrium coming on usually about two hours after lunch and lasting well into the evening. At times she felt nauseated; she very rarely vomited, and when she did the vomitus consisted of slightly sour, undigested, recently eaten food. The patient gradually developed an almost complete aversion to food and ate only small amounts of fat-free food; often she ate only toast for dinner. Four weeks prior to admission she noticed that the urine was dark brown, and the stools pale. She soon became jaundiced and the skin began to itch. The jaundice deepened, and the abnormal colored urine and stools persisted to the time of admission. During the illness her bowels remained regular, and only occasionally did she require Epsom salts for the relief of mild constipation. She had lost 10 pounds in weight during the previous three months. She believed that recently the abdomen and ankles had begun to swell.

The patient's mother died at fifty-five years of age with carcinoma of the breast. Two sisters had had hysterectomies done because of menorrhagia. Four years prior to admission the patient was sterilized by x-rays, because of persistent metrorrhagia; she had no further bleeding but continued to have a vaginal discharge and occasional pain in the right lower quadrant of the abdomen. Two years prior to admission the uterus, tubes and ovaries were removed for "fibroids."

Physical examination disclosed a thin, deeply jaundiced woman who appeared restless. The scleras were deeply jaundiced. There were many excoriations about the trunk, numerous small (1 to 2 mm.) purpuric spots about the knees and small "spider angiomas" of the arms, face, neck and thorax. The lungs and heart were normal. The liver edge was felt three fingerbreadths below the costal margin in the epigastrium. A mass that descended to the umbilicus on inspiration was believed to be an enlarged gall bladder. No tenderness was elicited. There was slight pitting edema at the ankles.

The blood pressure was 90 systolic, 55 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a hemoglobin of 10.9 gm. per 100 cc. and a white-cell count of 9600. The urine was acid, had a specific gravity of 1.020 and showed a + test for albumin and a +++ test for bile; the sediment contained amorphous urates and 6 white cells and 6 epithelial cells per high-power field. A blood Hinton test was negative. The prothrombin time was normal. The total protein was 5.0 gm. per 100 cc., and the bilirubin 12.3 mg. direct and 17.5 mg. indirect. The stool was light brown in color and guaiac negative in four examinations. The sedimentation rate was 16, 32, 44 and 49 mm. in fifteen, thirty, forty-five and sixty minutes respectively. A gastrointestinal series demonstrated a normal stomach and esophagus. The duodenal cap was large, and the tip was narrowed, apparently by an extrinsic band or blood vessel crossing it. The second portion of the duodenum showed no constant defects or evidence of rigidity of the wall.

After two weeks of preoperative preparation, including administration of water-soluble vitamin K and glucose-saline infusions, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. AUSTIN BRUES: This appears to be a classic case of carcinoma of the head of the pancreas. I shall therefore discuss it from the point of view of seeing whether any other diagnosis will fit with the history as given.

The age of the patient is consistent with that diagnosis, the average age in most series being the late fifties. The prodromal gastrointestinal symptoms without pain and with anorexia and weight loss are common, weight loss being extremely marked in certain cases of carcinoma of the head of the pancreas. At the time the symptoms appeared the patient had progressive jaundice, which became intense, with itching. The enlarged liver and the enlarged gall bladder, according to Courvoisier's law, indicate a constantly progressive lesion low down in the biliary system. The patient had a high bilirubin, direct and indirect, an elevated sedimentation rate and a normal prothrombin time. One might expect the prothrombin time to be elevated in jaundice; however, if the lesion produced obstruction primarily, the liver might

*On leave of absence.

have been able to maintain a normal blood prothrombin level for a period of some weeks.

I should say that the chief observation not in line with this diagnosis is that of spider angiomas, which are seen characteristically in cirrhosis of the liver, and may be observed a long time before the cirrhosis becomes manifest in other ways. They also have an endocrinologic angle, since they may appear during pregnancy and may be increased, when already present in patients with hepatic cirrhosis, by the administration of estrogen. It has been suggested that spider angiomas represent loss of liver function. Since the cirrhotic liver is unable to destroy or metabolize estrogen, this vicarious endometrial manifestation occurs in the skin. It is worth remarking incidentally that this woman was sterilized first by x-rays and then by ovariectomy. In line with the theory mentioned, it might be supposed that the angiomas antedated these procedures. At any rate, they suggest, but by no means prove, that the liver may have suffered chronic low-grade damage or was cirrhotic.

Another observation not quite in line with the diagnosis is that the stools were light brown. The obstruction therefore was not complete. That may have been an erroneous judgment; such things can occur. The obstruction may not have been incomplete, although anatomic considerations make it likely that once carcinoma of the head of the pancreas gives obstruction it shortly becomes complete, and that is what usually happens, unless there are anomalous or accessory bile ducts.

The low plasma protein and ankle edema may have been due to faulty nutrition; along with spider angiomas they might suggest a long-standing, low-grade hepatic insufficiency, but there is nothing else to indicate it. The prothrombin time was normal, and I am merely going to make the suggestion that there might have been some chronic liver damage unrelated to the main lesion. The slight albuminuria is consistent with jaundice.

Among the other diagnostic possibilities worth suggesting, the first is something associated with a low-grade chronic cirrhosis that would give these manifestations. The best of these probably is hepatoma. In that case the mass thought to have been gall bladder would be the tumor. The jaundice would be due to intrahepatic obstruction, and this would account for the small amount of bile in the stool. On the whole I think that is improbable. Carcinoma of the gall bladder might be considered. In that case the mass would be the carcinoma and again the obstruction would be intrahepatic from metastases high in the biliary system. Furthermore, I cannot rule out obstruction from some uncommon cause, such as fibrosis of the pancreas, lymphoma or metastases to periportal nodes compressing the bile duct. The fact that there was no palpable spleen is against lymphoma. I am against common-duct stone: Courvoisier's law is against it, as is the absence of pain and the steadily progressive nature of the jaundice. A common-duct stone can occur in a small percentage of cases without one of these anomalous findings, but from the laws of probability it seems extremely unlikely that these three unusual features could occur together. Carcinoma of the ampulla or of the duodenum I disfavor because of the absence of blood in the stool. My final diagnosis is carcinoma of the head of the pancreas.

Dr. Chester M. Jones: It seems to me that it is entirely probable that this woman had cirrhosis. Only a rare case with spider angiomas fails to have cirrhosis, excluding those cases observed in pregnant women. I think that this woman had severe liver damage. We do not know what the serum albumin was. The liver was certainly enlarged, and ankle edema and ascites were present. The fact that the patient had brown stools makes it conceivable that the whole clinical picture was due to intrahepatic disease alone. We have had cases of acute hepatic insufficiency with brown stools, a palpable liver, abdominal pain and fever. The important thing is that a definite diagnosis was not possible and therefore that exploration was indicated. I believe that carcinoma of the pancreas is less likely as a diagnosis than acute hepatic insufficiency or chronic liver disease with superimposed hepatoma.

Dr. Benjamin Castleman: You are basing all your conclusions on the spider angiomas?

Dr. Jones: Not entirely, but they furnish important evidence. The facts that there was color in the stool and that the patient had ascites and edema cannot be overlooked.

Dr. Arthur W. Allen: I should like to add that, for some reason or other, the types of obstructive jaundice that give brown stools or intermittently brown stools are much more apt to be associated with malignant disease than with any other type of biliary obstruction. I do not know why. Frequently a little bile goes through in cases of carcinoma, particularly of the papilla.

Dr. Castleman: Possibly that can be explained by the fact that the carcinoma often becomes necrotic, sloughs off and thus partially relieves the obstruction. It is seen more commonly in carcinoma of the papilla than in carcinoma of the head of the pancreas because the necrotic tumor may slough into the duodenum.

Dr. Greene Fitzhugh: This patient was operated on because her jaundice increased. We considered peritoneoscopy, but the jaundice increased

so rapidly that we thought it wiser to go ahead and do something about it.

DR. JONES: As I have said, the important thing here was to make the decision and not the diagnosis. But, in a case of this sort, one has to be prepared for liver disease as well as something outside the liver.

DR. RICHARD H. WALLACE: At operation the mass was a greatly distended gall bladder. The common duct was about 3 cm. in diameter. A mass was felt in the head of the pancreas. Fortunately we could make a diagnosis very readily because the tumor had extended through into the duodenum, or perhaps it started there, there being an area about 3 cm. in diameter with a central crater in the region of the papilla of Vater. We were able to resect the head of the pancreas with the proximal two thirds of the duodenum, and fortunately we could deliver the end of the duodenum beneath the mesenteric vessels and suture it to the end of the dilated common duct and were conveniently able to anastomose the end of the stomach to the side of the jejunum, making only two anastomoses. The patient had a smooth convalescence and is well today so far as we know.

DR. BRUES: Did you observe *typical* spider angiomas?

DR. WALLACE: She had what I consider to be spider angiomas.

DR. JONES: The pulsating sort?

DR. WALLACE: I am not sure of that.

DR. CASTLEMAN: How did the liver look?

DR. WALLACE: It was the enlarged, greenish liver that one sees with obstructive jaundice.

CLINICAL DIAGNOSIS

Carcinoma of head of pancreas.

DR. BRUES'S DIAGNOSIS

Carcinoma of head of pancreas.

ANATOMICAL DIAGNOSES

Adenocarcinoma of duodenum, involving the papilla of Vater, with extension to the pancreas and with metastases to the regional lymph nodes.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: We received a section of duodenum, 10 cm. long, with the attached head of the pancreas. On the mucosa of the duodenum surrounding the papilla of Vater was a large ulcerating tumor 3 cm. in diameter, with raised borders and a central ulceration. In the center of the crater was the opening of the common bile duct, which was markedly narrowed. The bile duct above the constriction was dilated. This tumor proved to be an adenocarcinoma that had extended through the duodenal wall to involve the surface and a very small portion of the pancreas. There is no doubt in my mind that the tumor was primary in the duodenum rather than in the pancreas. The regional lymph nodes were enlarged and hard and were filled with metastatic carcinoma. These were close to the head of the pancreas and were probably what was believed to have been the mass within the pancreas at operation.

CASE 29302

PRESENTATION OF CASE

A forty-four-year-old single woman entered the hospital because of profuse menstrual bleeding of a year's duration.

Menarche occurred at eleven years, and prior to the present illness, periods occurred regularly, with a twenty-eight-day cycle, and lasted five days. During menstruation the flow was moderate, requiring two napkins a day. On the fourth or fifth day she often had mild abdominal cramps. Approximately one year prior to admission the patient noticed gradual increase in the amount and duration of menstrual bleeding. About four months before entry her periods began to occur every twenty-four or twenty-five days and each lasted eighteen to twenty-one days. During the first two weeks she frequently passed small and moderate-sized blood clots. During the year of illness she suffered with a "bearing down" sensation in the pelvis but there were no changes in bowel or urinary habits and no weight loss. The last menstrual period began thirteen days prior to admission and flow continued to the day of admission.

The family and past histories were noncontributory. During the week prior to admission she had had an upper respiratory infection, from which she had recovered without sequelae.

Physical examination disclosed a well-developed and well-nourished woman who seemed quite comfortable. The pharynx was slightly congested, and the tonsils slightly enlarged. There was a soft, blowing systolic murmur audible over the entire precordium, best heard in the mitral area. The lungs were normal. A firm, slightly tender, irregular mass was felt in the lower abdomen. Vaginal examination under ether disclosed a normal-appearing cervix and a small vagina. The uterus was large but freely movable, and the vaults were negative.

The blood pressure was 125 systolic, 70 diastolic. The temperature, pulse and respirations were normal.

The blood was normal. The urine was bloody. A blood Hinton test was negative.

An operation was performed on the second hospital day.

Differential Diagnosis

Dr. John Rock: It is important throughout the history to note the terminology used in reference to the bleeding. It was profuse menstrual bleeding, which does not indicate what is commonly called "metrorrhagia." There is no suggestion of intermenstrual bleeding. The description makes me believe that this was polyhypermenorrhea and not dysfunctional flow or metrorrhagia.

"During the first two weeks she frequently passed small and moderate-sized blood clots." There was therefore some derangement of menstruation.

We are not told how large the abdominal mass was or where it was located in the abdomen, except that it was in the lower abdomen. It may have been on one side or the other, or very large or only palpable just above the symphysis. The fact that the vagina was small suggests that the vagina might have been encroached upon. The patient was unmarried; perhaps the vagina was normally small. We are told that the uterus was large, but we do not know how large — perhaps 6 or 7 cm. wide and 4 or 5 cm. thick or it might have reached up to the umbilicus. There was a mass in the abdomen, which may have been the uterus, but nothing was felt in either vault.

There was no blood dyscrasia to account for the polyhypermenorrhea. The urine was bloody, but if it was a voided specimen one would expect it to be bloody because the patient was flowing when she came in.

As I have said, we have to account for polyhypermenorrhea occurring in a forty-four-year-old woman that was associated with a mass in the lower abdomen and an enlarged uterus. Polyhypermenorrhea, that is, periods occurring at intervals shorter than the classic twenty-eight days, is not uncommon in a woman forty-four years old. Even excessive flow is not uncommon, but such marked prolongation of the periods indicates some pathology. So we might consider that it probably was due to whatever made the mass in the lower abdomen and enlarged the uterus. Following Cabot's instruction to make one diagnosis cover as many situations as possible, we had better say that the mass in the abdomen was the enlarged uterus. One can account for the bleeding perhaps by polyps, which prolong flow and result in the formation of clots. But polyps usually do not enlarge the uterus. Fibroids are of course the first thought that one would have to consider to account for all these things, probably multiple fibroids, because the mass in the lower abdomen was irregular. The patient could have had sarcoma, with or without fibroids, or she could have had endometriosis of the uterus itself. Endometriosis of the uterus is not uncommon and it does cause enlargement, which may be irregular; it usually does not cause intermenstrual flowing but increases in the amount and prolongation of the flow. It may also give enlargement of the uterus that is sufficient to be felt above the symphysis.

Then of course there is cancer. I think it is impossible to make a particular diagnosis here. Cancer in a forty-four-year-old woman sufficient to cause enlargement of the uterus and mass in the lower abdomen would have certainly given more bleeding than this patient had, and a different kind of bleeding.

We have to assume that the tumor was the uterus and that the ether examination was accurate. It is easy to mistake a tumor of either ovary for one of the uterus, and often an operation for fibroids is performed, because statistically they are the commonest cause of enlargement of the uterus, only to find that the tumor is a contiguous one of the ovary and not an outgrowth from the uterus.

Because the bleeding was of the menstrual variety we have to limit the diagnosis to fibroids or endometriosis of the uterus. How can we distinguish between these two? I do not know. Fibroids commonly give no symptoms whatever. They are troublesome only because of their size.

I think one was bound to operate on this patient with a working diagnosis of fibroids of the uterus but with the possibility of finding endometriosis or possibly sarcoma.

Dr. Joe V. Meigs: I think it is only fair to tell Dr. Rock that the patient did have a mass on one side.

Dr. Rock: If the mass on one side could be considered a tumor of the ovary then we must consider a tumor that does not interfere with ovulation. I do not know any tumor of the ovary that gives enough estrogen to increase flow without interfering with ovulation. But if the uterus is really enlarged in a woman of forty-four, we must assume some extra stimulation in the uterus, and therefore this patient might have had a granulosal-cell tumor of the ovary or, again, endometriosis of both the ovary and the uterus.

Dr. Meigs: I think the diagnoses that we made before we operated on the patient were fibroids and endometriosis. We knew there was a mass on the right side, which Dr. Rock did not know. I did not curet her because I was going to do a total removal of the uterus anyway.

At operation I found a cystic lobulated mass the size of an orange in the right ovary. One of the cysts had ruptured and there was a moderate amount of clear, free fluid in the abdomen. The whole uterus and the right ovary and tube were removed. My habit is to open the uterus before closing the abdominal wall, but this one time I did not do it. We had the patient's abdomen partially closed, when I realized I had not looked at the ovary or uterus. I stopped and opened the ovary, and much to my surprise, there were papillary areas and soft tissue inside. When I opened the uterus I found similar soft granular tissue on the endometrium, which made me think that the tumor had metastasized to the right ovary. I reopened the wound and removed the other tube and ovary.

The patient also had fibroids of the uterus and endometriosis of the pelvis.

Clinical Diagnoses

Fibroid of uterus.
Endometriosis.

Dr. Rock's Diagnosis

Uterine fibroid?
Endometriosis?

Anatomical Diagnoses

Adenoacanthoma of uterus, with metastasis to right ovary.
Leiomyomas of uterus.
Endometriosis of uterosacral ligament.

Pathological Discussion

Dr. Benjamin Castleman: We received three separate specimens. First the right ovary and tube and uterus, then the other ovary and tube and finally a small piece of tissue that had been removed from the pelvic floor.

Dr. Meigs: The left uterosacral ligament.

Dr. Castleman: The ovary was cystic, as Dr. Meigs has said, but the tissue inside was not really papillary. There was a mass of soft, friable tumor, which on section proved to be exactly the same as the tumor in the fundus of the uterus, an adenoacanthoma, that is, parts of tumor were adenocarcinomatous and other parts showed squamous-cell change or epidermoid carcinoma. This type of tumor is quite common in the body of the uterus, and I believe has a poorer prognosis than the straight adenocarcinoma.

Dr. Meigs: I should not say that. If it is treated with radiation, the outlook is poor, but if treated with surgery the results are fairly good.

Dr. Castleman: Just about the same as those in adenocarcinoma?

Dr. Meigs: Yes.

Dr. Castleman: If one finds a tumor in the ovary and one in the uterus it is often difficult to tell which is primary. The fact that this tumor was an adenoacanthoma proves that it was primary in the uterus. I do not believe that we have ever seen a primary adenoacanthoma of the ovary.

Dr. Meigs: Dr. Richard H. Miller had a case of primary adenoacanthoma of the ovary here years ago; nothing was found in the endometrium.

Dr. Castleman: The uterus also contained large fibroids, and the small piece of tissue removed from the uterosacral ligament showed endometriosis. So the patient had all three diseases.

Dr. Meigs: The tumor in the uterus was not localized to one area but filled the entire endometrial cavity. This made me think that the metastasis was from the endometrium to the ovary and not from the ovary to the endometrium.

Dr. Castleman: Why did you not do a curettage first, Dr. Meigs?

Dr. Meigs: If I am going to remove the entire uterus, I do not believe it is necessary; furthermore, if cancer is present a curettage may spill tumor. The uterus, however, must be opened before closing the abdominal incision.

Dr. Castleman: I have never been convinced that a curettage will implant tumor lower down. If metastases do occur in the vagina, I believe that they get there via the lymphatics.

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AWARD TO DOCTOR JOSLIN

To have been awarded the Distinguished Service Medal and Award of the American Medical Association and thus to be placed in the group of outstanding physicians that includes Hektoen, Herrick and Chevalier Jackson is an honor of which any man may justly be proud, and we of New England may similarly be proud that the recipient is Dr. Elliott P. Joslin.

A simple man of tireless energy and boundless enthusiasm, he has devoted his life to the treatment of diabetes mellitus. He has systematically trained the patient in knowledge of the disease so that life may be prolonged and health preserved. He could not have become such an outstanding specialist had he not had extensive general clinical experience abroad and later on the wards of the Boston City Hospital. He could never have acquired such detailed knowledge of diabetes had he not possessed infinite patience and been endowed with the ability to prevail against seemingly hopeless odds. His success would have been far less had he not recognized unconsciously that "the secret of the care of the patient is caring for the patient."

We congratulate Dr. Joslin on his achievement, and we hope that he may for many years continue the work for which so many thousands give thanks.

THE SYMBOL OF BUREAUCRACY

Physicians, with few exceptions, have been well treated so far as gasoline rationing is concerned, and their privileges have usually not been abused. They have been recognized as a hard-working, essential group of men and women, with more than average social consciousness and conscience. There has always been a tendency, in fact, to idealize their position in the community, to sentimentalize a little over their devotion to duty and their appetite for hardship and to grant them indulgence, as a class, on that account.

The fact is not to be lost sight of, however, that extra gasoline is not given as a reward for merit but as a means of enabling the physician to perform his functions in the community as efficiently as possible. He is made thereby, not a pampered idol, but a trusted public servant. The very nature of his services and the unpredictability of their character make it imperative that he should have his mode of transportation at hand. If he is permitted to have his recreation,—and the most zealous bureaucrat would hardly deny it to him,—he must have his car with him, if he is to stay on call. In all other ways he is an A-card holder, subject to the same restrictive regulations, the same lack of privilege and the same penalties that the owner of a so-called "pleasure car" enjoys.

The whole question of gasoline rationing merits

a serious review for here, in the minds of many who still cherish the idea of the rights of the individual, bureaucracy has committed one of its most serious blunders. It is not that gasoline rationing is unneeded; it is undoubtedly a stern necessity, recognized as such and accepted as such by the vast majority of citizens. It is the inability of bureaucracy to distinguish between the right and the wrong ways of directing a democratic people that is disquieting. To apportion the residue of gasoline that is left over after the necessities of war and the welfare of the public have been cared for is a reasonable procedure, even if the share of each person is only a gill a month. However, to set spies among the people to determine how each shall use his microscopic share, or suffer penalty, is quite different, and one of the most amazing things that has taken place on these shores since the Stamp Act engendered in the minds of a nation the idea of freedom from oppression.

It sometimes seems as if there were fixed in the collective mind of bureaucracy not only the idea that gasoline must be saved, but that in the saving thereof the people must be scourged. One can see rising in the form of a fuel director the spirit of Cotton Mather, purging the citizens of their devils and burning the witches at the stake.

MEDICAL EPONYM

Wintrich's Phenomenon

This is described by M. Anton Wintrich (1812–1882) in the section "Krankheiten der Respirationsorgane [Diseases of the Organs of Respiration]," in the first section of the fifth volume of Virchow's *Handbuch der speciellen Pathologie und Therapie* (Erlangen, 1854). A portion of the translation follows:

> The change in pitch of the tympanitic note over superficially situated cavities, connected via the bronchi with the trachea, larynx, mouth and so forth, by a continuous column of air, is a very pretty phenomenon. If the patient closes his mouth or swallows, thus narrowing or closing the opening of the larynx by lowering the epiglottis, the tympanitic note immediately becomes fainter . . . and deeper, and vice versa [when he opens his mouth].

R. W. B.

OBITUARY

WILLIAM FESSENDEN WESSELHOEFT

1862-1943

Dr. William Fessenden Wesselhoeft died of coronary disease and arteriosclerosis on June 27, 1943, at the Massachusetts Memorial Hospitals. He was born in Boston, March 5, 1862, and graduated from Harvard College in 1884; having rowed on the freshman crew and played varsity football. After graduating from Harvard Medical School in 1887, he took postgraduate courses at the Rotunda in Dublin, and in Vienna. He was the third William Wesselhoeft in line to practice medicine in Boston.

His grandfather received his medical degree at the University of Jena in 1820. Owing to membership in the Burschenschaft League and his volunteering as field surgeon to help the Greeks in their struggle for freedom, he was forced by Prussia and Austria to take refuge in Switzerland, where, for two years, he was demonstrator of anatomy at the University of Basel. On being warned that his extradition was sought, he walked all the way to Antwerp, where he took ship for New York and settled in Siegersville, Pennsylvania, in 1824. Thus he was one of the forerunners of those many political refugees from Germany who came over in great numbers with Karl Schurz in 1848, and the many more who have followed in this past decade. Through the influence of fellow refugees, Beck and Follen, Dr. William was asked to consider a position dealing with physical education at Harvard College, but this never materialized. He became interested in homeopathy and was one of the founders of what is now the Hahnemann Medical College in Philadelphia. He moved to Boston in 1842 and, as the story goes, was refused admission to the Massachusetts Medical Society on the grounds that he failed to bleed a case of typhoid fever. His brother, Robert Wesselhoeft, likewise a physician refugee, founded the "water cure" in Brattleboro, Vermont. This was the origin of a family of physicians in New England that found in homeopathy something more to their taste than the bleeding, blistering and purging so much in vogue at that time.

William Fessenden Wesselhoeft was the son of William Palmer Wesselhoeft, a graduate of Harvard Medical School in 1857 and an ardent homeopathist of the irreconcilable, high-dilution school, with a strong personality and advanced views regarding fresh air and the value of a mixed diet. The son espoused the hygienic views of the father, but lacking any true enthusiasm for the homeopathic method he took up surgery, working his

way up through the grades to the position of surgeon at the Massachusetts Memorial Hospitals and professor of clinical surgery at Boston University School of Medicine. He introduced a new surgical knot and devised a method of sterilizing catgut that was long in use at the Massachusetts Memorial Hospitals and elsewhere.

In World War I, with the rank of lieutenant colonel and as commanding officer of Base Hospital No. 44, he took this unit to France and served with it at Pouges les Eaux. He was a member of the Boston Surgical Society and a fellow of the American College of Surgeons. He never joined the Massachusetts Medical Society, a last flicker of protest handed down from a generation that exhibited a lively hostility.

Dr. Wesselhoeft married Emily Bradley, of Boston and Brattleboro, Vermont, who died in 1931. He is survived by four daughters: Margetta, widow of the late Dr. Bigelow, formerly commissioner of health of Massachusetts and Superintendent of the Massachusetts General Hospital; Susan, wife of Mr. Renouf Russell; Alice, wife of the honorable Leverett Saltonstall, governor of Massachusetts; and Emily, wife of Colonel William A. Barron, Jr., chief-of-staff of the First Service Command. He is also survived by thirteen grandchildren, two of whom are now serving in the Marines, three in the Navy and one in the Army. There are five great grandchildren.

Besides his many relatives, Dr. Wesselhoeft leaves behind him a large number of devoted patients and a host of colleagues who, as former students and subordinates, cherish the memory of his idealism for professional honesty, his spirit of service and his sympathetic manner at the bedside.

C. W.

MISCELLANY

"THE DOCTOR'S AUTOMOBILE"

Under the above title, the following statement, signed by Dr. Emery M. Potter, president of the Providence Medical Association, appeared in the July issue of *Medical News*, the official bulletin of the association. It is such an honorable and fair appeal that further comment seems unnecessary.

* * *

In the present-day practice of medicine the doctor finds his automobile an extremely necessary and vital instrument. Consequently the publication recently of rules and regulations by the Office of Price Administration to clarify the driving permitted and prohibited under the ban on so-called "pleasure driving" has caused much comment and speculation among the profession. The question arises as to how a doctor may pursue his regular routine and at the same time have his automobile accessible for emergencies without violating the OPA restrictions.

First let it be clearly understood that the Rhode Island OPA authorities are sympathetic with the problem which faces the doctor, and they are clearly cognizant of the fact that of all civilian groups the doctors of medicine — particularly those who are subject at all times to demands to administer to the sick, to respond to civilian disasters, to serve the Civilian Defense program, or to meet any general threat to the health of our community — have an imperative need to have their automobiles available in order to answer emergency calls promptly.

The OPA authorities here are fully aware of the shortage of doctors in the State owing to the withdrawals to meet the demands of the armed forces. Therefore they are particularly anxious to avoid the prosecution of any doctor for the violation of the rules of driving. But this desire to protect the health of the citizens and at the same time not to inconvenience the doctors of the State calls for a corresponding sincere co-operation by each physician. To date that co-operation has not been forthcoming at all times.

Several fundamental factors must be considered by the doctor as he justifies the use of his automobile for reasonable nonprofessional driving in order that he may have his car accessible for his personal use for emergency calls.

First — The doctor must realize that his professional calling places him in a preferred class, and he is obligated not to abuse the privileges accorded him. If the patient is denied the right to drive to the beach, or to drive to and from a summer home, then the doctor too must forego the same pleasures.

Second — While relaxation from strenuous work is essential for everyone, the doctor as well as the patient, the auto driving involved to reach recreational centers cannot in all fairness be more for one than for the other. Reasonable driving, even for social calls, may be undertaken by the doctor in order that he may have his automobile at hand for emergency hospital or sick calls, but the doctor must not misinterpret what constitutes reasonable driving under such circumstances.

Third — No doctor should embarrass his professional colleagues, nor should he antagonize public opinion, by flagrant violation of the OPA rules and regulations under the excuse of a physician's privilege to operate an automobile. Open violations of the restrictions certainly should merit penalty for all persons equally.

Fourth — The gasoline shortage in this area is far more critical than the average person realizes, and unless the situation eases in the next few weeks as the result of public co-operation, far more drastic restrictions, for doctors as well as for everyone else, are in the offing. No doctor should be guilty of abetting a black market under any circumstances.

Fifth — Remember we are still in an all-out war which will be won or lost by the way we fight it on the home front.

With these facts in mind you should be well guided by your conscience as you decide whether you are truly justified as a citizen aiding the war effort — not as a doctor exercising a special privilege — to use your automobile for nonprofessional driving.

CORRESPONDENCE

TAX-SUPPORTED MEDICAL CARE

To the Editor: The following letter addressed to all boards of public welfare and bureaus of old-age assistance in the State has been sent out this week. Each appointed city or town physician, and each physician who provides medical care for recipients of public assistance in any category, should obtain a copy of this formulary from the board of public welfare of the town in which he practices. The boards will greatly appreciate co-operation from physicians in the form of close adherence to the items on the formulary in their prescriptions. The boards will be able to provide physicians with any information that they may wish to obtain in regard to the formulary.

B. W. MANDELSTAM, M.D.
Medical Adviser

Department of Public Welfare
Division of Aid and Relief
State House
Boston

* * *

Gentlemen:

Administrators of public assistance have had many problems in connection with the provision of drugs for recipients of public assistance. Because of these difficulties the State Department of Public Welfare decided to compile a formulary. The formulary will be used by the department in reimbursing local boards of public welfare, but local boards will continue to deal directly with recipients, pharmacists and doctors.

The formulary has been compiled after a study of formularies of a number of hospitals, with suggestions from pharmacists as to those drugs most frequently dispensed. The list of drugs in the formulary, and the prices, have been approved respectively by the physicians' advisory committee and the druggists' advisory committee to the medical adviser of the State Department of Public Welfare.

With very few exceptions the list is composed of drugs that are standard *United States Pharmacopeia*, and not proprietary, products. Proprietary names have been listed in a number of instances, with a cross reference to the *U.S.P.* drug which is equivalent. The list has been prepared in alphabetical form for convenience. Revision will be made from time to time, depending on changes in price or on demand by physicians for additions.

The department will not reimburse local boards for drugs not on this list, unless prior approval has been obtained from the district office of the department. The price paid for any medication on the list will not be greater than the price listed therein. Every effort has been made to adjust quantities and prices so that physicians can prescribe sufficient medication to last for the whole interval between visits.

There are two types of formulary—one with prices and one without. The former is for the use of druggists who are providing medicine to recipients of public assistance. That without prices is for the use of physicians who are providing medical services to such recipients. Local boards of public welfare may secure the needed number of each type from their district office.

Where the recipient is allowed to purchase drugs from any pharmacist, or from a limited number of pharmacists, the mechanism of billing for the drugs depends on the local board of public welfare. Arrangements should be made between the druggist and the local board for the proper method of billing the recipient or the board.

Further information will be furnished from the Department of Public Welfare through the district office.

ARTHUR G. ROTCH
Commissioner

Department of Public Welfare
State House
Boston

BOOK REVIEW

Electrophoresis of Proteins and the Chemistry of Cell Surfaces. By Harold A. Abramson, Laurence S. Moyer and Manual H. Gorin. 8°, cloth, 341 pp., with 155 illustrations. New York: Reinhold Publishing Corporation, 1942. $6.00.

This book deals with a rapidly expanding field of investigation, which is of growing importance in medical science. The fact that charged particles (including cells, bacteria and protein molecules) move in an electric field has long been appreciated, but only recently has it been put to use through the development of the Tiselius and similar instruments. With proteins, electrophoretic methods may be used to estimate the quantities of components of different mobilities in a mixture such as plasma, to separate these components and to demonstrate the identity or heterogeneity of a chemically isolated fraction.

Many clinically useful tests (albumin-globulin ratio, sedimentation rate, Takata–Ara reaction, colloidal-gold test) depend on variations in the protein pattern. Whereas plasma albumin migrates as a unit, the globulins can be separated into at least three components, so that electrophoresis has much potential clinical value. Certain antibodies are recognized by the great increase in quantity of a protein component occurring in hyperimmune serums and by its disappearance after absorption by the specific antigen. The antibody components are identical with the gamma globulin or fall between the gamma and beta globulins on the electrophoretic diagram. Consequently, the supposition has been made that the increase in plasma gamma globulin occurring in sarcoidosis and amyloidosis may represent antibody formation. Furthermore, electrophoretic methods have been of value in controlling the separation of trophic hormones from extracts of the anterior pituitary gland and in proving their purity.

The book details many other investigations, including chapters on latex and on the surface chemistry of cells and a discussion of therapy by electrophoretic transport of drugs and allergens through the skin.

A book covering the rising curve of research in a new field can hardly be written in leisure, and suffers in being out of date before the ink is dry; and a more compendious index might have increased its usefulness. These inadequacies are small beside the value of a much-needed monograph. The first half of the book (theory and methods) is indispensable to those who undertake electrophoretic studies or the critical evaluation of those of other men. The entire book is worthy of perusal by clinicians and investigators who wish to keep abreast of the biophysical aspects of disease.

NOTICES

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, AUGUST 5

THURSDAY, AUGUST 5

*10:00–11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

MONDAY, AUGUST 9

*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, AUGUST 10

*12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

2:00–4:00 p.m. Myasthenia gravis clinic. Out Patient Department, Massachusetts General Hospital.

WEDNESDAY, AUGUST 11

*12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

SEPTEMBER 8–11. American Congress of Physical Therapy. Page 32, issue of July 1.

OCTOBER 11–22. 1943 Graduate Fortnight of the New York Academy of Medicine. Page 32, issue of July 1.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Outline of Roentgen Diagnosis: An orientation in the basic principles of diagnosis by the roentgen method. By Leo G. Rigler, M.B., M.D., professor of radiology, University of Minnesota, Minneapolis. Second edition. 4°, cloth, 321 pp., with 254 illustrations. Philadelphia: J. B. Lippincott Company, 1943. $6.50.

Five years have elapsed since the first edition of this book, which has necessitated a thorough revision of the text. The type has been completely reset, and much of the text rewritten, incorporating new procedures, such as roentgenkymography, body-section roentgenography and myelography for herniation of the intervertebral disk, as well as other new procedures. New material on sarcoidosis, brucellosis, erythroblastic anemia and the technic and value of fluoroscopy has been added. The work is intended as an outline for the teaching of roentgen diagnosis, and the particular needs of the teacher and student have been kept in mind.

(Books Received continued on page ix)

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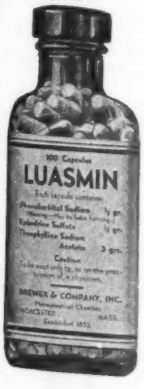

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*A New Type of Medication to Be Used in Bronchial Asthma and Other Allergic Conditions. *New England Journal of Medicine* 223:843–846, 1940.

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Selection of Officer Candidates. By William L. Woods, M.D.; Lucien Brouha, M.D.; and Carl C. Seltzer, Ph.D. In collaboration with Clark W. Heath, M.D., Arlie V. Bock, M.D., Dr. Phil., John M. Flumerfelt, M.D., and Frederic L. Wells, Ph.D. 8°, paper, 50 pp., with 10 figures and 4 tables. Cambridge: Harvard University Press, 1943. 75 cents.

This pamphlet describes the method for selection of young men for training as officers in the armed forces. It is based on experience and knowledge gained during the past four years and the study of undergraduates at Harvard College. The group studied were healthy, sound and intelligent. The method also takes into account the results of consultation with military commanders concerning qualities of leadership. An attempt has been made to reduce procedures to comparatively simple and minimum forms, which are consistent with reasonable accuracy. Because of the urgency of the wartime needs, it has been considered advisable to eliminate complete personality studies and to depend on a combination of three technics: measurements of physical fitness, personality and body build. Information derived from these technics is used in addition to the initial medical examination and all other data obtained from the candidates.

The report describes the rationale, results and details of the tests used. The pamphlet is divided into two parts: discussion of the methods that embody the physical-fitness test, the short interview and the consideration of the masculine component; and personnel and training requirements for administration of the test. The second part is devoted to detailed instructions for carrying out the tests. Tables and figures, giving examples of good and poor officer candidates, as well as physical fitness and masculine component ratings, are included.

Clinical Laboratory Diagnosis. By Samuel A. Levinson, M.D., director of laboratories and pathologist, Research and Educational Hospitals, Chicago, and professor of pathology and assistant professor of medicine, University of Illinois College of Medicine; and Robert P. MacFate, Ch.E., M.S., Ph.D., assistant director of laboratories, Research and Educational Hospitals, Chicago, and assistant professor of pathology, University of Illinois College of Medicine. Second edition. 3°, cloth, 980 pp., with 156 illustrations, 92 tables and 15 plates. Philadelphia: Lea and Febiger, 1943. $10.00.

This second edition has been thoroughly revised and brought up to date by the addition of over 100 pages of text. New methods have been added, and old ones deleted.

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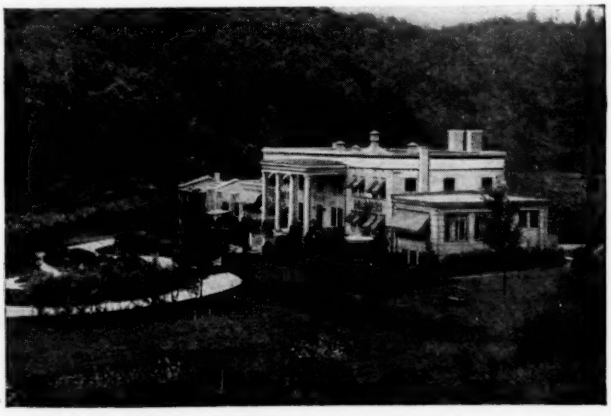

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